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FILE 'USPAT' ENTERED AT 11:10:55 ON 15 MAR 1999
              Welcome to MESSENGER (APS Text) at USPTO
                                                                              WELCOME
                                                                                              TΩ
                                                                                                    THE
                                                                        U.S.
                                                                                PATENT
                                                                                              TEXT FILE
       The USPTO production files are current through:
       MARCH 09,1999 for U.S. Patent Text Data.
                                                            => activate comclm/q
       MARCH 09,1999 for U.S. Current Classification Data.L1
                                                                            QUE ((LIBRAR#### OR ARRAY# OR IDENTIF####
                                                            OR COLLECTION#
       MARCH 09,1999 for U.S. Patent Image Data.
                                                                             OR COMBINATORIAL OR RANDOM OR MIXTURES OR
                                                            PLURALITIES) (6
                                                                            A) (MOLECULE# OR CHEMICAL# OR CHEMIST#####
                                                           OR SYNTHESI####
                                                                            OR COMBINATORIAL))/CLM NOT PY<1989
     AFTER PRODUCTION HOURS (AT 10:00 P.M.) ON WEDNESDAY,
                                                          => set high off
01/27/99.
     SEVERAL PTONET DEVICES WILL BE RECONFIGURED TO ENHANCESET COMMAND COMPLETED
     NETWORK OPERATIONS. USERS OF PATENT EXAMINER SEARCH
                                                           => s 11
     MUST RE-BOOT THEIR INDIVIDUAL DESKTOP WORKSTATIONS AT
THE
                                                                     2020 LIBRAR####/CLM
     START OF THE BUSINESS DAY ON THURSDAY, 01/28/99 TO
                                                                    64196 ARRAY#/CLM
INSURE
                                                                    53354 IDENTIF####/CLM
     THAT NECESSARY FILES ON THEIR WORKSTATION GET UPDATED.
                                                                    17436 COLLECTION#/CLM
THIS
                                                                      615 COMBINATORIAL/CLM
     WILL ENSURE IMMEDIATE AND ACCURATE ACCESS TO ALL OF
                                                                    21925 RANDOM/CLM
THE
                                                                    67910 MIXTURES/CLM
     PATENT EXAMINER SEARCH TOOLS. THANK YOU FOR YOUR
                                                                     5189 PLURALITIES/CLM
COOPERATION
                                                                    26662 MOLECULE#/CLM
  * * * * *
                                                                    34400 CHEMICAL#/CLM
                                                                      676 CHEMIST#####/CLM
          * PLEASE USE 305-9000 FOR NEW TELEPHONE NUMBER *
                                                                    14656 SYNTHESI####/CLM
                                                                      615 COMBINATORIAL/CLM
                                                                     1421 ((LIBRAR#### OR ARRAY# OR IDENTIF#### OR
                                                           COLLECTION# OR COM
                                                          * BTN
                                                                          ATORIAL OR RANDOM OR MIXTURES OR
                   Help Desk --> 703-305-9000
                                                           PLURALITIES) (6A) (MOLECULE#
                                                                           CHEMICAL# OR CHEMIST##### OR SYNTHESI####
                                                           OR COMBINATORIAL
      The Help Desk is staffed for APS support 7
                                                           11/
days/week.
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        Monday through Friday:
                                    6:30am - 9:00pm
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                                                                      932 ((LIBRAR#### OR ARRAY# OR IDENTIF#### OR
        Saturday, Sunday, Holidays: 8:30am - 5:00 pm
                                                           COLLECTION# OR COM
                                                           BIN
                                                                          ATORIAL OR RANDOM OR MIXTURES OR
                                                           PLURALITIES) (6A) (MOLECULE#
      The Help Desk staff at this number will handle all
                                                            OR
APS
                                                                           CHEMICAL# OR CHEMIST##### OR SYNTHESI####
       related questions.
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                                                                          CLM NOT PY<1989
      >>>>>> NEW SUNDAY HOURS !!! <<<<<<<
                                                           => set high on
                                                           SET COMMAND COMPLETED
      The APS is available:
                                                           => s 12 and (cleav#### or releas### or separat####) (5a)
                                                           (support# of link#)
              6:30am - 9:00pm Monday through Friday
                                                                    46424 CLEAV####
              7:30am - 5:00pm Saturday, Sunday, Holidays
                                                                   537964 RELEAS###
                                                                  1283318 SEPARAT####
                                                                   814989 SUPPORT#
                                                                   182732 LINK#
        APS is unavailable Thanksgiving Day, Christmas
                                                                     1731 SUPPORT# OF LINK#
Dav.
                                                                            (SUPPORT#(1W)LINK#)
        and New Year's Day.
                                                                       27 (CLEAV#### OR RELEAS### OR SEPARAT###) (5A)
                                                           (SUPPORT# OF L
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INK
                                                                       2825 SUPPORT# OF LINK?
                # 1
                                                                              (SUPPORT#(1W)LINK?)
 L3
              O L2 AND (CLEAV#### OR RELEAS### OR
                                                                        384 (CLEAV#### OR RELEAS### OR SEPARAT####) (P)
 SEPARAT####) (5A) (SUPPOR
                                                             (SUPPORT# OF LI
Т#
                                                             NK?
               OF LINK#)
                                                                        6 L2 AND (CLEAV#### OR RELEAS### OR
 => s 12 and (cleav#### or releas### or separat####) (10a)
                                                             SEPARAT####) (P) (SUPPORT
 (support# of link?)
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         46424 CLEAV####
        537964 RELEAS###
                                                             => s 15 not 14
       1283318 SEPARAT###
        814989 SUPPORT#
                                                                          5 L5 NOT L4
         379703 LINK?
          2825 SUPPORT# OF LINK?
                                                             => d 1-5 cit kwic
                  (SUPPORT#(1W)LINK?)
           104 (CLEAV#### OR RELEAS### OR SEPARAT####)
 (10A) (SUPPORT# OF
                                                             1. 5,846,839, Dec. 8, 1998, Methods for hard-tagging an
LIN
                                                             encoded
                                                             synthetic library; Mark A. Gallop, et al., 436/518;
                                                             435/7.1; 436/85, 501,
             1 L2 AND (CLEAV#### OR RELEAS### OR
SEPARAT###) (10A) (SUPPO
                                                             528, 531 [IMAGE AVAILABLE]
RT#
                OF LINK?)
                                                            US PAT NO:
                                                                            5,846,839 [IMAGE AVAILABLE]
                                                                                                                    L6:
                                                            1 of 5
=> d cit hit
                                                             DETDESC:
1. 5,877,214, Mar. 2, 1999, Polyaryl-poly(ethylene glycol) DETD(13)
supports for
solution-phase combinatorial synthesis; Ronald M. Kim,
                                                             Reversible covalent **cleavable** linkages can be used to
514/571, 576, 650;
                                                            attach the
562/42, 426, 452, 470; 564/337, 346, 348, 355; 568/62, 607, molecules to the support. Examples of suitable reversible
609 [IMAGE
                                                            chemical
AVAILABLE]
                                                            linkages include (1) a sulfoester linkage provided by,
                                                            e.g., a thiolated
US PAT NO:
               5,877,214 [IMAGE AVAILABLE]
                                                        L4: tagged-molecule and a N-hydroxy-succinimidyl **support**,
1 of 1
                                                            which
                                                            **linkage** can be controlled by adjustment of the ammonium
SUMMARY:
                                                            hydroxide
                                                            concentration; (2) a benzylhydryl or benzylamide linkage
                                                            provided by,
BSUM(51)
                                                            e.g., a. .
                                                                           from Sigma), which linkage can be
 By the term "synthon" is meant any chemical moiety which
                                                            controlled by
                                                            adjustment of the DTT (dithiothreitol) concentration; and
synthetically manipulated to permit its covalent linking to (4) linkers
                                                            which can be **cleaved** with a transition metal (e.g.
a support or
to another synthon. To facilitate the separation of the
                                                            HYCRAM).
synthon from the
polyvalent support it is preferred that the synthon be
                                                            2. 5,751,629, May 12, 1998, Remotely programmable matrices
attached via a
                                                            with
chemically **cleavable** linker. Upon **cleavage** from thememories; Michael P. Nova, et al., 365/151, 153 [IMAGE
**support**,
                                                            AVAILABLE ]
the **linked** synthons comprise discrete molecular
entities which may be
                                                            US PAT NO:
                                                                           5,751,629 [IMAGE AVAILABLE]
                                                                                                                    L6:
analyzed for their biological activity or physiochemical
                                                            2 of 5
properties, or
which may be subjected to further chemical modification.
                                                            SUMMARY:
=> d date
                                                            BSUM(8)
                                                             Following hybridization of a detection oligonucleotide
                                                        L4: with a target,
1 of 1
                                                            the resulting signal-generating hybrid molecules must be
TITLE:
               Polyaryl-poly(ethylene glycol) supports for **separated**
solution-phase
                                                            from unreacted target and detection oligonucleotides. In
                                                            order to do so,
                 combinatorial synthesis
US PAT NO:
               5,877,214
                                        DATE ISSUED:
                                                       Mar. many of the commonly used assays immobilize the target.
2, 1999

    adducts

               [IMAGE AVAILABLE]
                                                            formed in solution [see, e.g., EP 276,302 and Gingeras et
APPL-NO:
               08/923,299
                                        DATE FILED:
                                                        Sep.al. (1989)
4, 1997
                                                            Proc. Natl. Acad. Sci. USA 86:1173]. Solid **supports**
                                                            with **linked**
=> s 12 and (cleav#### or releas### or separat####) (p)
                                                            oligonucleotides are also used in methods of affinity
(support# of link?)
                                                            purification.
                                                            Following hybridization or affinity purification, however,
         46424 CLEAV####
                                                            i f
        537964 RELEAS###
                                                            identification of the linked. . .
       1283318 SEPARAT####
        814989 SUPPORT#
                                                          '3. 5,663,046, Sep. 2, 1997, Synthesis of combinatorial
```

libraries; John

379703 LINK?

```
J. Baldwin, et al., 435/6, 7.1; 436/501, 518, 531, 533;
                                                            which can be **cleaved** with a transition metal (i.e.
530/333, 334;
                                                            HYCRAM).
536/18.5, 25.3 [IMAGE AVAILABLE]
                                                            => d 1-5cit date
US PAT NO:
               5,663,046 [IMAGE AVAILABLE]
                                                        L6:
3 of 5
                                                             '1-5CIT' IS NOT A VALID FORMAT FOR FILE 'USPAT'
                                                            ENTER DISPLAY FORMAT (CIT):end
SUMMARY:
                                                            => d 1-5 cit date
BSUM(71)
 The . . Y. Compound 7 is then either exposed to UV
liaht
                                                            1. 5,846,839, Dec. 8, 1998, Methods for hard-tagging an
(.about.360 nm) in a lower alkanol such as MeOH to
                                                            encoded
**cleave** the
                                                            synthetic library; Mark A. Gallop, et al., 436/518;
protected form of the compounds of Formula II from the
                                                            435/7.1; 436/85, 501,
**support**/**linker** complex or first treated with
                                                            528, 531 [IMAGE AVAILABLE]
TFA/thioanisole/EDT
to remove the protecting groups on the R.sup.2 sidechains
                                                                                                                    L6:
and then
                                                            1 of 5
exposed to UV light in a lower alkanol such as MeOH to
                                                                           Methods for hard-tagging an encoded
                                                            TITLE:
**cleave**
                                                            synthetic library
compound II. ##STR3##
                                                                           5,846,839
                                                            US PAT NO:
                                                                                                     DATE ISSUED:
                                                                                                                    Dec.
                                                            8, 1998
4. 5,604,097, Feb. 18, 1997, Methods for sorting
                                                                           [IMAGE AVAILABLE]
polynucleotides using
                                                            APPL-NO:
                                                                           08/577,203
                                                                                                     DATE FILED:
                                                                                                                    Dec.
oligonucleotide tags; Sydney Brenner, 435/6; 536/25.4
                                                            22, 1995
[IMAGE AVAILABLE]
                                                            2. 5,751,629, May 12, 1998, Remotely programmable matrices
US PAT NO:
               5,604,097 [IMAGE AVAILABLE]
                                                        L6: with
4 of 5
                                                            memories; Michael P. Nova, et al., 365/151, 153 [IMAGE
                                                            AVAILABLE]
DETDESC:
                                                                                                                    1.6:
DETD(41)
                                                            2 of 5
                                                            TITLE:
                                                                           Remotely programmable matrices with memories
 Tag complements may be used with the solid phase support
                                                            US PAT NO:
                                                                           5,751,629
                                                                                                     DATE ISSUED:
                                                                                                                    May
that they are
                                                            12, 1998
synthesized on, or they may be **separately** synthesized
                                                                           [IMAGE AVAILABLE]
                                                            APPL-NO:
and attached to
                                                                           08/484,504
                                                                                                     DATE FILED:
                                                                                                                    Jun.
a solid phase support for use, e.g. as disclosed by Lund et7, 1995
                                                            REL-US-DATA:
al. Nucleic
                                                                           Continuation-in-part of Ser. No. 428,662,
Acids Research,. . . employed depends on the conditions Apr. 25, 1995.
under which
the tags are used. For example, in applications involving 3. 5,663,046, Sep. 2, 1997, Synthesis of combinatorial
                                                            libraries; John
successive
processing with enzymes, **supports** and **linkers** that J. Baldwin, et al., 435/6, 7.1; 436/501, 518, 531, 533;
                                                            530/333, 334;
steric hinderance of the enzymes and that facilitate access 536/18.5, 25.3 [IMAGE AVAILABLE]
to substrate
are preferred. Exemplary linking moieties are disclosed.
                                                                                                                    L6:
                                                            3 of 5
                                                            TITLE:
                                                                           Synthesis of combinatorial libraries
5. 5,549,974, Aug. 27, 1996, Methods for the solid phase US PAT NO:
                                                                           5,663,046
                                                                                                     DATE ISSUED:
                                                                                                                    Sep.
synthesis of
                                                            2, 1997
thiazolidinones, metathiazanones, and derivatives thereof;
                                                                           [IMAGE AVAILABLE]
Christopher P.
                                                            APPL-NO:
                                                                           08/263,804
                                                                                                     DATE FILED:
                                                                                                                    Jun.
Holmes, 428/403, 406, 407, 411.1, 426, 457; 544/54; 548/18222, 1994
[IMAGE
AVAILABLE]
                                                            4. 5,604,097, Feb. 18, 1997, Methods for sorting
                                                            polynucleotides using
US PAT NO:
               5,549,974 [IMAGE AVAILABLE]
                                                       L6: oligonucleotide tags; Sydney Brenner, 435/6; 536/25.4
5.of 5
                                                            [IMAGE AVAILABLE]
DETDESC:
                                                                                                                    L6:
                                                            4 of 5
DETD(143)
                                                            TITLE:
                                                                           Methods for sorting polynucleotides using
                                                            oligonucleotide
Reversible . . . Examples of suitable reversible
                                                                             tags
chemical linkages
                                                            US PAT NO:
                                                                           5,604,097
                                                                                                     DATE ISSUED:
                                                                                                                    Feb.
include (1) a sulfoester linkage provided by, e.g., a
                                                            18, 1997
thiolated
                                                                           [IMAGE AVAILABLE]
                                                            APPL-NO:
tagged-molecule and a N-hydroxysuccinimidyl **support**,
                                                                           08/358,810
                                                                                                     DATE FILED:
                                                                                                                    Dec.
which
                                                            19, 1994
**linkage** can be controlled by adjustment of the ammoniumREL-US-DATA:
                                                                           Continuation-in-part of Ser. No. 322,348,
hydroxide
                                                            Oct. 13, 1994,
concentration; (2) an benzylhydryl or benzylamide linkage
                                                                             abandoned.
provided by,
               from Sigma), which linkage can be
                                                            5. 5,549,974, Aug. 27, 1996, Methods for the solid phase
controlled by
                                                            synthesis of
adjustment of the DTT (dithiothreitol) concentration; and
                                                            thiazolidinones, metathiazanones, and derivatives thereof;
(4) linkers
                                                            Christopher P.
```

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Holmes, 428/403, 406, 407, 411.1, 426, 457; 544/54; 548/182
ITMAGE
                                                           => d 1-150 cit date
AVAILABLE]
                                                                50 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER
                                                       L6: EXCEEDS ANSWER SET
5 of 5
                                                           STZE
TITLE:
               Methods for the solid phase synthesis of
                                                           ENTER ANSWER NUMBER OR RANGE (1):1-50
thiazolidinones,
                 metathiazanones, and derivatives thereof
US PAT NO:
               5,549,974
                                        DATE ISSUED:
                                                      Aug. 1. 5,877,214, Mar. 2, 1999, Polyaryl-poly(ethylene glycol)
27, 1996
                                                           supports for
               [IMAGE AVAILABLE]
                                                           solution-phase combinatorial synthesis; Ronald M. Kim,
APPL-NO:
               08/265,090
                                        DATE FILED:
                                                       Jun. 514/571, 576, 650;
23, 1994
                                                           562/42, 426, 452, 470; 564/337, 346, 348, 355; 568/62, 607,
                                                           609 [IMAGE
=> d saved
                                                           AVAILABLE]
                 CREATED
NAME
                              NOTES/TITLE
                 -----
                              -----1 of 50
                                                           TITLE:
                                                                          Polyaryl-poly(ethylene glycol) supports for
COMCLM/O
                02 FEB 1999
                             QUERY CREATED IN FILE USPAT
                                                          solution-phase
COMLIB/Q
                12 MAY 1998
                             QUERY CREATED IN FILE USPAT
                                                                            combinatorial synthesis
PCTUS9715493/L
                08 OCT 1997
                             5 L-NUMBERS
                                                           US PAT NO:
                                                                          5,877,214
                                                                                                   DATE ISSUED:
SAVEALL/L
                 17 FEB 1998 7 L-NUMBERS
                                                           2. 1999
TEST/Q
                01 OCT 1997 QUERY CREATED IN FILE USPAT
                                                                          [IMAGE AVAILABLE]
                                                           APPL-NO:
                                                                          08/923,299
                                                                                                   DATE FILED:
=> activate comlib/q
                                                           4. 1997
                QUE (LIBRAR#### OR ARRAY# OR MULTIP###### 2. 5,876,930, Mar. 2, 1999, Hybridization assay using
L7
OR COLLECTION#
                                                           self-quenching
                OR COMBINATORIAL OR RANDOM) (6A) (MOLECULE# fluorescence probe; Kenneth J. Livak, et al., 435/6, 5,
OR CHEMICAL#
                                                           91.1, 91.2;
               OR CHEMIST##### OR SYNTHE##### OR
                                                           536/24.3, 24.32, 24.33, 25.3, 25.32, 26.6 [IMAGE AVAILABLE]
COMBINATORIAL)
=> set high off
                                                           2 of 50
                                                           TITLE:
SET COMMAND COMPLETED
                                                           fluorescence
```

Hybridization assay using self-quenching => s 17US PAT NO: 5,876,930 DATE ISSUED: 2. 1999

22089 LIBRAR#### [IMAGE AVAILABLE] 193467 ARRAY# APPL-NO: 08/558,303 DATE FILED: Nov. 568027 MULTIP##### 15, 1995 114017 COLLECTION# REL-US-DATA: Continuation of Ser. No. 340,558, Nov. 16, 4323 COMBINATORIAL 1994, Pat. No. 157587 RANDOM 5,538,848. 176703 MOLECULE# 438541 CHEMICAL# 3. 5,874,532, Feb. 23, 1999, Method for solution phase 96056 CHEMIST####

synthesis of 373500 SYNTHE##### oligonucleotides and peptides; Wolfgang Pieken, et al., 4323 COMBINATORIAL 530/338, 322; 14398 (LIBRAR#### OR ARRAY# OR MULTIP###### OR 536/25.3, 25.34; 562/433 [IMAGE AVAILABLE] COLLECTION# OR COM L9:

US PAT NO:

23, 1999

APPL-NO:

8, 1997

ATORIAL OR RANDOM) (6A) (MOLECULE# OR 3 of 50 CHEMICAL# OR CHEMIST## TITLE: Method for solution phase synthesis of ### oligonucleotides

OR SYNTHE##### OR COMBINATORIAL) and peptides

=> set high on

SET COMMAND COMPLETED

=> s 18 and (cleav#### or releas### or separat####) (p)

(support# of link?)

46424 CLEAV#### 537964 RELEAS### 1283318 SEPARAT#### 814989 SUPPORT# 379703 LINK? 2825 SUPPORT# OF LINK?

F LINK?)

(SUPPORT#(1W)LINK?)

384 (CLEAV#### OR RELEAS### OR SEPARAT####) (P) TITLE: (SUPPORT# OF LI

NK? 50 L8 AND (CLEAV#### OR RELEAS### OR SEPARAT###) (P) (SUPPORT # O

4. 5,874,214, Feb. 23, 1999, Remotely programmable matrices with memories; Michael P. Nova, et al., 435/6; 365/151, 153; 422/58, 68.1,

5,874,532

08/780,517

[IMAGE AVAILABLE]

L9:

Mar.

Sep.

L9:

Mar.

Feb.

Jan.

DATE ISSUED:

DATE FILED:

82.01, 82.05, 82.12; 424/422, 489; 435/7.8, 7.92 [IMAGE AVAILABLE]

L9: 4 of 50 Remotely programmable matrices with memories

US PAT NO: 5,874,214 DATE ISSUED: Feb. 23. 1999 [IMAGE AVAILABLE]

APPL-NO: 08/538.387 DATE FILED: Oct. 3, 1995 REL-US-DATA: Continuation-in-part of Ser. No. 480,147, Jun. 7, 1995,

```
Ser. No. 484,486, Jun. 7, 1995, Ser. No.
 484,504, Jun.
                                                             9. 5,859,233, Jan. 12, 1999, Synthons for synthesis of
                  7, 1995, Pat. No. 5,751,629, Ser. No.
                                                             oligonucleotide
 480,196, Jun. 7,
                                                             N3-P5 phosphoramidates; Bernard L. Hirschbein, et al.,
                  1995, Ser. No. 473,660, Jun. 7, 1995, and 536/26.1, 26.12,
 Ser. No.
                                                             26.14 [IMAGE AVAILABLE]
                  428,662, Apr. 25, 1995, Pat. No.
5,741,462, said Ser.
                                                                                                                      L9:
                  No. 480,147, Ser. No. 484,486, Ser. No. 9 of 50
484,504, Ser.
                                                             TITLE:
                                                                             Synthons for synthesis of oligonucleotide
                  No. 480,196, and Ser. No. 473,660, each
                                                             N3-P5
 Ser. No. is a
                                                                               phosphoramidates
                  continuation-in-part of Ser. No. 428,662. US PAT NO:
                                                                             5,859,233
                                                                                                       DATE ISSUED:
                                                                                                                      Jan.
                                                             12, 1999
5. 5,872,244, Feb. 16, 1999, 3' protected nucleotides for
                                                                             [IMAGE AVAILABLE]
enzvme
                                                             APPL-NO:
                                                                             08/771,789
                                                                                                       DATE FILED:
                                                                                                                      Dec.
catalyzed template-independent creation of phosphodiester
                                                             20. 1996
bonds; Andrew
                                                             REL-US-DATA:
                                                                             Continuation-in-part of Ser. No. 663,918,
C. Hiatt, et al., 536/26.26, 26.6, 26.7 [IMAGE AVAILABLE]
                                                             Jun. 14, 1996,
                                                                               which is a continuation-in-part of Ser.
                                                         L9: No. 603,566,
5 of 50
                                                                               Feb. 21, 1996, Pat. No. 5,684,143.
TITLE:
                3' protected nucleotides for enzyme
catalyzed
                                                             10. 5,846,841, Dec. 8, 1998, Motif Libraries; Nikolai
                 template-independent creation of
                                                             Sepetov, et al.,
phosphodiester bonds
                                                             436/518; 435/7.1; 436/501; 530/333, 334 [IMAGE AVAILABLE]
US PAT NO:
               5,872,244
                                         DATE ISSUED:
                                                         Feb.
16, 1999
                                                                                                                      L9:
                [IMAGE AVAILABLE]
                                                             10 of 50
APPL-NO:
               08/486.535
                                         DATE FILED:
                                                         Jun. TITLE:
                                                                            Motif Libraries
7, 1995
                                                             US PAT NO:
                                                                            5,846,841
                                                                                                      DATE ISSUED:
                                                                                                                      Dec.
REL-US-DATA:
               Continuation-in-part of Ser. No. 300,484,
                                                             8, 1998
Sep. 2, 1994.
                                                                             [IMAGE AVAILABLE]
                                                             APPL-NO:
                                                                            08/754,878
                                                                                                      DATE FILED:
                                                                                                                      Nov.
6. 5,864,031, Jan. 26, 1999, Process for preparing 5-
                                                             22, 1996
dithio-modified
                                                             REL-US-DATA:
                                                                            Continuation of Ser. No. 246,435, May 20,
oligonucleotides; Sandra E. Russo-Rodriguez, et al.,
                                                             1994, abandoned.
536/25.34, 25.3
[IMAGE AVAILABLE]
                                                             11. 5,846,839, Dec. 8, 1998, Methods for hard-tagging an
                                                             encoded
                                                        L9: synthetic library; Mark A. Gallop, et al., 436/518;
6 of 50
                                                             435/7.1; 436/85, 501,
TITLE:
               Process for preparing 5-dithio-modified
                                                             528, 531 [IMAGE AVAILABLE]
oligonucleotides
US PAT NO:
               5,864,031
                                         DATE ISSUED:
                                                                                                                      L9: .
26, 1999
                                                             11 of 50
               [IMAGE AVAILABLE]
                                                             TITLE:
                                                                            Methods for hard-tagging an encoded
APPL-NO:
               08/282,383
                                         DATE FILED:
                                                        Jul. synthetic library
29, 1994
                                                             US PAT NO:
                                                                            5,846,839
                                                                                                      DATE ISSUED:
                                                                                                                      Dec.
                                                             8, 1998
7. 5,863,722, Jan. 26, 1999, Method of sorting
                                                                            [IMAGE AVAILABLE]
polynucleotides; Sydney
                                                             APPL-NO:
                                                                            08/577,203
                                                                                                      DATE FILED:
                                                                                                                     Dec.
Brenner, 435/6; 536/24.3 [IMAGE AVAILABLE]
                                                             22, 1995
                                                        L9: 12. 5,846,731, Dec. 8, 1998, Peralkylated oligopeptide
7 of 50
                                                             mixtures; Richard
TITLE:
               Method of sorting polynucleotides
                                                             A. Houghten, et al., 435/7.1, 7.2, 7.32; 436/501, 518, 536;
US PAT NO:
               5,863,722
                                         DATE ISSUED:
                                                        Jan. 530/323, 332,
26, 1999
                                                             333, 334, 345 [IMAGE AVAILABLE]
               [IMAGE AVAILABLE]
APPL-NO:
               08/485,105
                                         DATE FILED:
                                                        Jun.
                                                                                                                     L9:
7, 1995
                                                             12 of 50
REL-US-DATA:
               Continuation of Ser. No. 359,295, Dec. 19,
                                                             TITLE:
                                                                            Peralkylated oligopeptide mixtures
1994, which is
                                                             US PAT NO:
                                                                            5,846,731
                                                                                                      DATE ISSUED:
                                                                                                                     Dec.
                 a continuation-in-part of Ser. No.
                                                             8, 1998
322,348, Oct. 13,
                                                                            [IMAGE AVAILABLE]
                 1994, abandoned.
                                                             APPL-NO:
                                                                            08/079,144
                                                                                                      DATE FILED:
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                                                             17, 1993
8. 5,861,532, Jan. 19, 1999, Solid-phase synthesis of N-
alkyl amides;
                                                             13. 5,846,719, Dec. 8, 1998, Oligonucleotide tags for
Edward G. Brown, et al., 564/142; 436/85, 86; 564/133, 134, sorting and
135, 136,
                                                             identification; Sydney Brenner, et al., 435/6; 536/23.1,
137, 139 [IMAGE AVAILABLE]
                                                             24.2, 24.3, 25.4
                                                             [IMAGE AVAILABLE]
8 of 50
                                                                                                                     L9:
TITLE:
               Solid-phase synthesis of N-alkyl amides
                                                             13 of 50
US PAT NO:
               5,861,532
                                         DATE ISSUED:
                                                        Jan. TITLE:
                                                                            Oligonucleotide tags for sorting and
19, 1999
                                                             identification
               [IMAGE AVAILABLE]
                                                             US PAT NO:
                                                                            5.846.719
                                                                                                      DATE ISSUED:
                                                                                                                     Dec.
APPL-NO:
               08/813,019
                                         DATE FILED:
                                                        Mar. 8, 1998
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[IMAGE AVAILABLE]

4, 1997

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APPL-NO:
               08/659,453
                                        DATE FILED:
                                                         Jun. APPL-NO:
                                                                            08/731,362
                                                                                                      DATE FILED:
                                                                                                                      Oct.
6, 1996
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REL-US-DATA:
               Continuation-in-part of Ser. No. 358,810,
                                                             REL-US-DATA:
                                                                            Continuation-in-part of Ser. No. 670,713.
Dec. 19, 1994,
                                                             Jun. 18, 1996,
                Pat. No. 5,604,097, which is a
                                                                               and a continuation-in-part of Ser. No.
continuation-in-part of
                                                             393,318, Feb. 22,
                 Ser. No. 322,348, Oct. 13, 1994,
                                                                              1995, abandoned, which is a continuation-
abandoned.
                                                             in-part of Ser.
                                                                              No. 265,578, Jun. 23, 1994, abandoned.
14. 5,840,485, Nov. 24, 1998, Topologically segregated,
encoded solid
                                                             18. 5,808,045, Sep. 15, 1998, Compositions for enzyme
phase libraries; Michal Lebl, et al., 435/6, 7.1; 436/518; catalyzed
530/300, 323;
                                                             template-independent creation of phosphodiester bonds using
536/23.1 [IMAGE AVAILABLE]
                                                             protected
                                                             nucleotides; Andrew C. Hiatt, et al., 536/26.26, 26.7,
                                                         L9: 26.71, 26.72,
14 of 50
                                                             26.74, 26.8 [IMAGE AVAILABLE]
TITLE:
               Topologically segregated, encoded solid
phase libraries
                                                                                                                      1.9:
US PAT NO:
               5,840,485
                                         DATE ISSUED:
                                                        Nov. 18 of 50
24, 1998
                                                             TITLE:
                                                                            Compositions for enzyme catalyzed template-
               [IMAGE AVAILABLE]
                                                             independent
APPL-NO:
               08/249,830
                                         DATE FILED:
                                                                              creation of phosphodiester bonds using
26, 1994
                                                             protected
REL-US-DATA:
               Continuation-in-part of Ser. No. 68,327, May
                                                                              nucleotides
                                                                            5,808,045
27, 1993,
                                                             US PAT NO:
                                                                                                      DATE ISSUED:
                                                                                                                     Sep.
                 abandoned.
                                                             15, 1998
                                                                            [IMAGE AVAILABLE]
15. 5,824,793, Oct. 20, 1998, Solid phase synthesis of
                                                             APPL-NO:
                                                                            08/486,897
                                                                                                      DATE FILED:
                                                                                                                      Jun.
oligonucleotide
                                                             7, 1995
N3'-P5' phosphoramidates; Bernard L. Hirschbein, et al.,
                                                             REL-US-DATA:
                                                                            Continuation-in-part of Ser. No. 300,484,
536/25.34, 25.3,
                                                             Sep. 2, 1994,
25.33 [IMAGE AVAILABLE]
                                                                              abandoned.
                                                        L9: 19. 5,763,594, Jun. 9, 1998, 3' protected nucleotides for
15 of 50
                                                             enzvme
TITLE:
               Solid phase synthesis of oligonucleotide
                                                             catalyzed template-independent creation of phosphodiester
N3'-P5'
                                                             bonds: Andrew
                 phosphoramidates
                                                             C. Hiatt, et al., 536/25.3; 435/6; 536/25.1, 25.31, 25.32,
US PAT NO:
               5,824,793
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                                                        Oct. 25.33, 25.34,
20, 1998
                                                             26.1 [IMAGE AVAILABLE]
               [IMAGE AVAILABLE]
APPL-NO:
               08/663,918
                                         DATE FILED:
                                                        Jun.
                                                                                                                     L9:
14, 1996
                                                             19 of 50
REL-US-DATA:
               Continuation-in-part of Ser. No. 603,566,
                                                             TITLE:
                                                                            3' protected nucleotides for enzyme
Feb. 21, 1996,
                                                             catalyzed
                 Pat. No. 5,684,143.
                                                                              template-independent creation of
                                                            phosphodiester bonds
16. 5,821,130, Oct. 13, 1998, Combinatorial
                                                             US PAT NO:
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dihydrobenzopyran library;
                                                             9, 1998
John J. Baldwin, et al., 436/518, 523, 524, 525, 526, 527,
                                                                            [IMAGE AVAILABLE]
528, 529, 530,
                                                            APPL-NO:
                                                                            08/486,913
                                                                                                      DATE FILED:
                                                                                                                     Jun.
531; 564/183, 184, 186 [IMAGE AVAILABLE]
                                                             7, 1995
                                                            REL-US-DATA:
                                                                            Continuation-in-part of Ser. No. 300,484,
                                                        L9: Sep. 2, 1994.
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TITLE:
               Combinatorial dihydrobenzopyran library
                                                             20. 5,763,193, Jun. 9, 1998, Peralkylated oligopeptide
US PAT NO:
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                                         DATE ISSUED:
                                                        Oct. mixtures; Richard
13, 1998
                                                            A. Houghten, et al., 435/7.1, 7.2, 7.21; 436/501, 518
               [IMAGE AVAILABLE]
                                                             [IMAGE AVAILABLE]
APPL-NO:
               08/552.698
                                         DATE FILED:
                                                        Nov.
3, 1995
                                                                                                                     L9:
REL-US-DATA:
               Continuation-in-part of Ser. No. 436,120,
                                                            20 of 50
May 8, 1995,
                                                            TITLE:
                                                                            Peralkylated oligopeptide mixtures
                 abandoned, which is a continuation-in-partUS PAT NO:
                                                                            5,763,193
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of Ser. No.
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                 239,302, May 6, 1994, abandoned.
                                                                            [IMAGE AVAILABLE]
                                                            APPL-NO:
                                                                            08/577,846
                                                                                                      DATE FILED:
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17. 5,817,751, Oct. 6, 1998, Method for synthesis of
                                                            22, 1995
diketopiperazine
                                                            REL-US-DATA:
                                                                            Division of Ser. No. 257,782, Jun. 9, 1994,
and diketomorpholine derivatives; Anna Katrin Szardenings, Pat. No.
                                                                              5,480,971, which is a continuation-in-part
530/317, 334; 544/170 [IMAGE AVAILABLE]
                                                            of Ser. No.
                                                                              79,144, Jun. 17, 1993.
                                                        L9:
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                                                            21. 5,756,810, May 26, 1998, Process of preparing 3-nitro
TITLE:
               Method for synthesis of diketopiperazine andbenzoate
                 diketomorpholine derivatives
                                                            compounds in lower alkanol; John J. Baldwin, et al.,
US PAT NO:
               5,817,751
                                         DATE ISSUED:
                                                        Oct. 560/20, 23 [IMAGE
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AVAILABLE

6, 1998

[IMAGE AVAILABLE]

		L9:			Pyrrolidine-containing monomers and					
21 of 50 TITLE: compounds in	Process of preparing 3- lower	nitro benzoate		oligomers US PAT NO: 3, 1998	5,714,606	DATE ISSUED:	Feb.			
US PAT NO: 26, 1998	alkanol 5,756,810	DATE ISSUED:	Мау	APPL-NO: 15, 1996	[IMAGE AVAILABLE] 08/669,505	DATE FILED:	Aug.			
APPL-NO:	[IMAGE AVAILABLE] 08/714,065	DATE FILED:	Sep	PCT-NO: 0.11, 1995	PCT/US95/00356	PCT-FILED:	Jan.			
11, 1996 PCT-NO:	PCT/US95/03223	PCT-FILED:	Mar	.15, 1996		371-DATE:	Aug.			
10, 1995	•	371-DATE:				102(E)-DATE:	Aug.			
11, 1996		102(E)-DATE:	•	PCT-PUB-NO: .13, 1995	WO95/18792	PCT-PUB-DATE:	Jul.			
11, 1996 PCT-PUB-NO:	WO95/24186	PCT-PUB-DATE:	•	REL-US-DATA:	Continuation-in-part of	F Ser. No. 180,1	34,			
14, 1995		ICI-FOB-BAIL.	sep	.Jan. 11, 1994,	Pat. No. 5,519,134.					
matrices with	9, May 12, 1998, Remotely	-	2	26. 5,714,597, Feb. 3, 1998, Use of carbocation scavenger during oligonucleotide synthesis; Vasulinga Ravikumar, et al., 536/25.31, 25.3,						
			L9:		[IMAGE AVAILABLE]					
22 of 50 TITLE:	Remotely programmable m	atrices with mem	noria	s 26 of 50			L9:			
US PAT NO: 12, 1998	5,751,629	DATE ISSUED:		TITLE: oligonucleotic	Use of carbocation scav	venger during				
APPL-NO: 7, 1995	[IMAGE AVAILABLE] 08/484,504	DATE FILED:	Jun	.US PAT NO: 3, 1998	synthesis 5,714,597	DATE ISSUED:	Feb.			
REL-US-DATA:	Continuation-in-part of	Ser. No. 428,66	52,	·	[IMAGE AVAILABLE]					
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matrices with			1994, Pat. No.		, 2/1,181, Jul.	′•				
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23 of 50			L9:	AVAILABLE]						
TITLE: US PAT NO:	ITLE: Remotely programmable matrices with memorie S PAT NO: 5,741,462 DATE ISSUED: Apr						L9:			
21, 1998 APPL-NO:	[IMAGE AVAILABLE] 08/428,662	DATE FILED:	Anr	TITLE: US PAT NO: .3, 1998	Anti .alphagal screen 5,714,332	ing technique DATE ISSUED:	Feb.			
25, 1995				APPL-NO:	[IMAGE AVAILABLE] 08/740,166	DATE FILED:	Oct.			
24. 5,723,593 probe; Kenneth	l, Mar. 3, 1998, Self-que n	nching fluoresce	nce	22, 1996						
J. Livak, et a	al., 536/22.1, 23.1, 24.3	, 25.3, 25.32 [II	MAGE	multiple			or			
24 - 5 52		•	L9:	422/131, 130,						
24 of 50 TITLE:	Self-quenching fluoresc	ence probe		435/304.1, 305	.2; 530/333, 334 [IMAGE	AVAILABLE]				
US PAT NO: 3, 1998	5,723,591	DATE ISSUED:	Mar	28 of 50			L9:			
APPL-NO:	[IMAGE AVAILABLE] 08/559,405	DATE FILED:	Nov	TITLE: .simultaneous s	Apparatus and method fo	r multiple				
15, 1995 REL-US-DATA:	Continuation of Ser. No			US PAT NO: 30, 1997	5,702,672	DATE ISSUED:	Dec.			
1994, Pat. No. 5,538,848.				APPL-NO:	[IMAGE AVAILABLE] 08/540,512	DATE FILED:	Oct.			
25. 5,714,606, Feb. 3, 1998, Pyrrolidine-containing monomers and				10, 1995 REL-US-DATA:	Continuation-in-part of	Ser. No. 430,69	6,			
oligomers; Oscar L. Acevedo, et al., 544/243, 35, 102, 104, Pat. No. 5,612,002, which is a division of										
	299, 309, 311, 313, 314,	, 317, 335; 548/	Ser. No.	217,347, Mar. 24, 1994, abandoned, which						
	362.5, 364.1, 412, 413,	414, 440, 441, 4	is a division	of Ser. No. 12,557, Feb. 2, 1993, Pat. No.						
444, 446, 465, 466, 467, 518, AVAILABLE]	519, 523, 524, 530, 531,	, 542, 546 [IMAG	E	5,324,483,	which is a continuation-in-part of Ser.					
AVAILABLE] No. 958,383, Oct. 8, 1992, abandoned.										

Oct. 8, 1992, abandoned.

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29. 5,695,934, Dec. 9, 1997, Massively parallel sequencing TITLE:
                                                                              Selectively cleavabe linners based on
 of sorted
                                                              iminodiacetic acid
 polynucleotides; Sydney Brenner, 435/6; 536/24.3 [IMAGE
                                                                                esters for solid phase peptide synthesis
 AVAILABLE)
                                                              US PAT NO:
                                                                              5,635,598
                                                                                                       DATE ISSUED:
                                                                                                                       Jun.
                                                              3, 1997
                                                          L9:
                                                                              [IMAGE AVAILABLE]
 29 of 50
                                                              APPL-NO:
                                                                              08/263,289
                                                                                                       DATE FILED:
                                                                                                                       Jun.
 TITLE:
                Massively parallel sequencing of sorted
                                                              21, 1994
 polynucleotides
                                                              REL-US-DATA:
                                                                             Continuation-in-part of Ser. No. 81,997,
 US PAT NO:
                5,695,934
                                          DATE ISSUED:
                                                          Dec. Jun. 23, 1993,
 9, 1997
                                                                                abandoned, which is a continuation-in-part
                [IMAGE AVAILABLE]
                                                              of Ser. No.
 APPL-NO:
                08/359,295
                                          DATE FILED:
                                                          Dec.
                                                                                80,388, Jun. 21, 1993, abandoned:
 19, 1994
 REL-US-DATA:
                Continuation-in-part of Ser. No. 322,348,
                                                              34. 5,635,400, Jun. 3, 1997, Minimally cross-hybridizing
 Oct. 13, 1994,
                                                              sets of
                  abandoned.
                                                              oligonucleotide tags; Sydney Brenner, 435/320.1, 6;
                                                              536/22.1, 24.2 [IMAGE
 30. 5,688,997, Nov. 18, 1997, Process for preparing
                                                              AVAILABLE]
 intermediates for a
combinatorial dihydrobenzopyran library; John J. Baldwin,
                                                                                                                       L9:
 et al.,
                                                              34 of 50
 562/435; 435/7.1; 560/21 [IMAGE AVAILABLE]
                                                              TITLE:
                                                                             Minimally cross-hybridizing sets of
                                                              oligonucleotide tags
                                                         L9: US PAT NO:
                                                                             5,635,400
                                                                                                       DATE ISSUED:
                                                                                                                       Jun.
 30 of 50
                                                              3, 1997
 TITLE:
                Process for preparing intermediates for a
                                                                              [IMAGE AVAILABLE]
 combinatorial
                                                              APPL-NO:
                                                                             08/478,238
                                                                                                       DATE FILED:
                                                                                                                       Jun.
                  dihydrobenzopyran library
                                                              7, 1995
US PAT NO:
                5,688,997
                                          DATE ISSUED:
                                                                             Continuation of Ser. No. 358,810, Dec. 19,
                                                         Nov. REL-US-DATA:
18, 1997
                                                              1994, which is
                [IMAGE AVAILABLE]
                                                                               a continuation-in-part of Ser. No.
APPL-NO:
                08/482,488
                                          DATE FILED:
                                                         Jun. 322,348, Oct. 13,
7, 1995
                                                                               1994, abandoned.
REL-US-DATA:
                Division of Ser. No. 436,120, May 8, 1995,
which is a
                                                              35. 5,618,825, Apr. 8, 1997, Combinatorial sulfonamide
                  continuation-in-part of Ser. No. 239,302, library; John J.
May 6, 1994,
                                                              Baldwin, et al., 514/317, 330; 546/227, 229, 232, 233, 234,
                  abandoned.
                                                              235; 548/543,
                                                              556, 569 [IMAGE AVAILABLE]
31. 5,663,046, Sep. 2, 1997, Synthesis of combinatorial
libraries; John
                                                                                                                       L9:
J. Baldwin, et al., 435/6, 7.1; 436/501, 518, 531, 533;
                                                              35 of 50
530/333, 334;
                                                              TITLE:
                                                                             Combinatorial sulfonamide library
536/18.5, 25.3 [IMAGE AVAILABLE]
                                                             US PAT NO:
                                                                             5,618,825
                                                                                                       DATE ISSUED:
                                                                                                                      Apr.
                                                              8, 1997
                                                         L9:
                                                                             [IMAGE AVAILABLE]
31 of 50
                                                             APPL-NO:
                                                                             08/482,489
                                                                                                       DATE FILED:
                                                                                                                       Jun.
TITLE:
                Synthesis of combinatorial libraries
                                                              7, 1995
US PAT NO:
                5,663,046
                                         DATE ISSUED:
                                                         Sep. REL-US-DATA:
                                                                             Division of Ser. No. 212,024, Mar. 11, 1994.
2, 1997
                [IMAGE AVAILABLE]
                                                             36. 5,604,097, Feb. 18, 1997, Methods for sorting
APPL-NO:
                08/263.804
                                          DATE FILED:
                                                         Jun.polynucleotides using
22, 1994
                                                             oligonucleotide tags; Sydney Brenner, 435/6; 536/25.4
                                                             [IMAGE AVAILABLE]
32. 5,654,413, Aug. 5, 1997, Compositions for sorting
polynucleotides;
                                                                                                                      L9:
Sydney Brenner, 536/22.1; 435/6, 320.1; 536/24.2 [IMAGE
                                                             36 of 50
AVAILABLE]
                                                             TITLE:
                                                                             Methods for sorting polynucleotides using
                                                             oligonucleotide
                                                                               tags
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                                                             US PAT NO:
                                                                             5,604,097
                                                                                                       DATE ISSUED:
                                                                                                                      Feb.
TITLE:
               Compositions for sorting polynucleotides
                                                             18. 1997
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               5,654,413
                                         DATE ISSUED:
                                                         Aug.
                                                                             [IMAGE AVAILABLE]
5, 1997
                                                             APPL-NO:
                                                                             08/358,810
                                                                                                       DATE FILED:
                                                                                                                      Dec.
                [IMAGE AVAILABLE]
                                                             19, 1994
APPL-NO:
               08/484,712
                                         DATE FILED:
                                                         Jun. REL-US-DATA:
                                                                             Continuation-in-part of Ser. No. 322,348,
7. 1995
                                                             Oct. 13, 1994,
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               Continuation of Ser. No. 358,810, Dec. 19,
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1994, which is
                  a continuation-in-part of Ser. No.
                                                             37. 5,587,471, Dec. 24, 1996, Method of making
322,348, Oct. 13,
                                                             oligonucleotide
                 1994, abandoned.
                                                             libraries; Phillip D. Cook, et al., 536/25.3, 25.4, 25.41
                                                             [ IMAGE
33. 5,635,598, Jun. 3, 1997, Selectively cleavabe linners AVAILABLE]
based on
iminodiacetic acid esters for solid phase peptide
                                                                                                                      L9:
synthesis; Michal Lebl.
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et al., 530/334, 343, 345 [IMAGE AVAILABLE]
                                                             TITLE:
                                                                            Method of making oligonucleotide libraries
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                                                        L9: 24, 1996
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[IMAGE AVAILABLE]

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APPL-NO:
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                                                         Jan. Holmes, 428/403, 406, 407, 411.1, 426, 457; 544/54; 548/182
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                                                             [ IMAGE
                                                             AVAILABLE]
38. 5,567,391, Oct. 22, 1996, Apparatus for multiple
simultaneous
                                                                                                                      1.9:
synthesis; Sheila H. H. DeWitt, et al., 422/131, 130, 196; 41 of 50
435/304.1.
                                                             TITLE:
                                                                            Methods for the solid phase synthesis of
305.2 [IMAGE AVAILABLE]
                                                             thiazolidinones,
                                                                              metathiazanones, and derivatives thereof
                                                         L9: US PAT NO:
                                                                             5,549,974
                                                                                                      DATE ISSUED:
                                                                                                                      Auq.
38 of 50
                                                             27, 1996
TITLE:
               Apparatus for multiple simultaneous
                                                                             [IMAGE AVAILABLE]
synthesis
                                                             APPL-NO:
                                                                             08/265,090
                                                                                                      DATE FILED:
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               5,567,391
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22, 1996
                [IMAGE AVAILABLE]
                                                             42. 5,525,735, Jun. 11, 1996, Methods for synthesizing
APPL-NO:
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                                                         Jun.diverse
5, 1995
                                                             collections of pyrrolidine compounds; Mark A. Gallop, et
REL-US-DATA:
               Continuation of Ser. No. 430,696, Apr. 28,
                                                             al., 548/533;
1995, which is
                                                             435/7.92; 436/518; 530/323; 548/400, 406, 453, 517, 518,
                 a continuation of Ser. No. 217,347, Mar.
                                                             532, 536, 537,
24, 1994,
                                                             541, 560, 565, 566, 570, 577 [IMAGE AVAILABLE]
                  abandoned, which is a division of Ser. No.
12,557, Feb.
                                                                                                                      L9:
                 2, 1993, Pat. No. 5,324,483, Jun. 28,
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1994, which is a
                                                             TITLE:
                                                                            Methods for synthesizing diverse collections
                 continuation-in-part of Ser. No. 958,383, of
Oct. 8, 1992,
                                                                              pyrrolidine compounds
                 abandoned.
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                                                             11, 1996
39. 5,565,173, Oct. 15, 1996, Apparatus and method for
                                                                            [IMAGE AVAILABLE]
multiple
                                                             APPL-NO:
                                                                            08/354,309
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simultaneous synthesis; Sheila H. H. DeWitt, et al.,
                                                             12, 1994
422/131, 130, 196;
                                                             REL-US-DATA:
                                                                            Continuation-in-part of Ser. No. 264,136,
435/304.1, 305.2 [IMAGE AVAILABLE]
                                                             Jun. 22, 1994.
                                                        L9: 43. 5,510,476, Apr. 23, 1996, Carbocation scavenging
39 of 50
                                                             during
TITLE:
               Apparatus and method for multiple
                                                             oligonucleotide synthesis; Vasulinga Ravikumar, et al.,
simultaneous synthesis
                                                             536/25.31, 25.3,
US PAT NO:
               5,565,173
                                         DATE ISSUED:
                                                        Oct. 25.33, 25.34 [IMAGE AVAILABLE]
15, 1996
               [IMAGE AVAILABLE]
                                                                                                                     L9:
APPL-NO:
               08/461,998
                                         DATE FILED:
                                                        Jun. 43 of 50
5, 1995
                                                             TITLE:
                                                                            Carbocation scavenging during
REL-US-DATA:
               Continuation of Ser. No. 430,696, Apr. 28,
                                                             oligonucleotide synthesis
1995, which is
                                                             US PAT NO:
                                                                            5,510,476
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                 a continuation of Ser. No. 217,347, Mar.
                                                            23, 1996
24, 1994,
                                                                            [IMAGE AVAILABLE]
                 abandoned, which is a division of Ser. No. APPL-NO:
                                                                            08/271,181
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                                                             44. 5,480,971, Jan. 2, 1996, Peralkylated oligopeptide
                 continuation-in-part of Ser. No. 958,383, mixtures; Richard
Oct. 8, 1992,
                                                            A. Houghten, et al., 530/328, 329 [IMAGE AVAILABLE]
                 abandoned.
                                                                                                                     L9:
40. 5,554,501, Sep. 10, 1996, Biopolymer synthesis using
                                                            44 of 50
surface
                                                             TITLE:
                                                                            Peralkylated oligopeptide mixtures
activated biaxially oriented polypropylene; Peter J.
                                                            US PAT NO:
                                                                            5,480,971
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                                                                                                                     Jan.
Coassin, et al.
                                                             2. 1996
435/6; 436/63, 89, 94; 530/334; 536/25.3 [IMAGE AVAILABLE]
                                                                            [IMAGE AVAILABLE]
                                                            APPL-NO:
                                                                            08/257,782
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                                                        L9: 9, 1994
40 of 50
                                                            REL-US-DATA:
                                                                            Continuation-in-part of Ser. No. 79,144,
TITLE:
               Biopolymer synthesis using surface activated Jun. 17, 1993.
biaxially
                 oriented polypropylene
                                                             45. 5,403,711, Apr. 4, 1995, Nucleic acid hybridization
US PAT NO:
               5,554,501
                                         DATE ISSUED:
10, 1996
                                                            amplification method for detection of specific sequences in
               [IMAGE AVAILABLE]
                                                            which a
APPL-NO:
               08/145,939
                                         DATE FILED:
                                                        Oct. complementary labeled nucleic acid probe is cleaved; Joseph
29, 1993
                                                            A. Walder, et
REL-US-DATA:
               Continuation-in-part of Ser. No. 971,100,
                                                            al., 435/6, 91.2; 536/24.3 [IMAGE AVAILABLE]
Oct. 29, 1992,
                 abandoned.
                                                                                                                     L9:
                                                             45 of 50
41. 5,549,974, Aug. 27, 1996, Methods for the solid phase TITLE:
                                                                            Nucleic acid hybridization and amplification
```

method for

complementary

detection of specific sequences in which a

labeled nucleic acid probe is cleaved

E

synthesis of

Christopher P.

thiazolidinones, metathiazanones, and derivatives thereof;

US PAT NO: 5,403,711 DATE ISSUED: Apr. TITLE: Urine testing apparatus with urinary 4, 1995 sediment device [IMAGE AVAILABLE] US PAT NO: 5,137,031 DATE ISSUED: Aug. APPL-NO: 08/088,622 DATE FILED: Jul. 11, 1992 6, 1993 [IMAGE AVAILABLE] REL-US-DATA: Continuation of Ser. No. 757,555, Sep. 11, APPL-NO: 07/567,758 DATE FILED: Aua. 1991, 15, 1990 abandoned, which is a continuation of Ser. REL-US-DATA: Continuation-in-part of Ser. No. 408,547, No. 173,127, Sep. 18, 1989, Mar. 24, 1988, abandoned, which is a Pat. No. 5,024,238, and a continuation-incontinuation-in-part of Ser. No. 126,564, part of Ser. Nov. 30, 1987, No. 411,041, Sep. 22, 1989, Pat. No. abandoned. 4,953,561. 46. 5,324,483, Jun. 28, 1994, Apparatus for multiple 50. 4,636,463, Jan. 13, 1987, Antibodies to human simultaneous interleukin-2 induced synthesis; Donna R. Cody, et al., 422/131, 99, 101, 104 by synthetic polypeptides; Amnon Altman, et al., 435/7.92; [IMAGE AVAILABLE] 210/502.1; 424/85.2; 435/7.93, 7.94, 810, 975; 436/547, 808, 823; L9: 514/14; 530/300, 46 of 50 326, 327, 351, 387.9, 389.2; 930/10, 141, DIG.811 [IMAGE TITLE: Apparatus for multiple simultaneous AVAILABLEI synthesis US PAT NO: 5,324,483 DATE ISSUED: Jun. L9: 28, 1994 50 of 50 [IMAGE AVAILABLE] TITLE: Antibodies to human interleukin-2 induced by APPL-NO: 08/012,557 DATE FILED: Feb. synthetic 2. 1993 polypeptides REL-US-DATA: Continuation-in-part of Ser. No. 958,383, US PAT NO: 4,636,463 DATE ISSUED: Jan. Oct. 8, 1992, 13, 1987 abandoned. [IMAGE AVAILABLE] APPL-NO: 06/597,179 DATE FILED: Apr. 47. 5,286,789, Feb. 15, 1994, Solid phase multiple peptide5, 1984 David Okrongly, et al., 525/54.11, 54.1, 333.6, 350, 374, => s 18 and (cleav#### or releas### or separat####) (15a) 379; 530/333, (support# of link?) 334, 335, 815, 816 [IMAGE AVAILABLE] 46424 CLEAV#### L9: 537964 RELEAS### 47 of 50 1283318 SEPARAT#### TITLE: Solid phase multiple peptide synthesis 814989 SUPPORT# US PAT NO: 5,286,789 DATE ISSUED: Feb. 379703 LINK? 15, 1994 2825 SUPPORT# OF LINK? [IMAGE AVAILABLE] (SUPPORT#(1W)LINK?) APPL-NO: 08/041,901 130 (CLEAV#### OR RELEAS### OR SEPARAT####) DATE FILED: 2, 1993 (15A) (SUPPORT# OF REL-US-DATA: Continuation of Ser. No. 671,671, Mar. 19, LIN 1991, K?) abandoned, which is a continuation of Ser. L10 29 L8 AND (CLEAV#### OR RELEAS### OR No. 357,987, SEPARAT####) (15A) (SUPPO May 26, 1989, abandoned. RT# OF LINK?) 48. 5,256,549, Oct. 26, 1993, Purification of synthetic oligomers: => d 1-29 cit date kwic Michael S. Urdea, et al., 435/91.1, 91.3, 91.5; 530/334, 335, 336, 337, 344; 536/25.3, 25.31 [IMAGE AVAILABLE] 1. 5,877,214, Mar. 2, 1999, Polyaryl-poly(ethylene glycol) supports for L9: solution-phase combinatorial synthesis; Ronald M. Kim, 48 of 50 514/571, 576, 650; TITLE: Purification of synthetic oligomers 562/42, 426, 452, 470; 564/337, 346, 348, 355; 568/62, 607, US PAT NO: 5,256,549 DATE ISSUED: Oct. 609 [IMAGE 26, 1993 AVAILABLE] [IMAGE AVAILABLE] APPL-NO: 07/517.526 DATE FILED: Apr. L10: 27, 1990 1 of 29 REL-US-DATA: Continuation of Ser. No. 229,475, Aug. 3, TITLE: Polyaryl-poly(ethylene glycol) supports for 1988, abandoned, solution-phase which is a continuation-in-part of Ser. combinatorial synthesis No. 891.789. US PAT NO: 5,877,214 DATE ISSUED: Mar. Jul. 30, 1986, abandoned, which is a 2, 1999 continuation-in-part of Ser. No. 845,290, [IMAGE AVAILABLE] Mar. 28, 1986, APPL-NO: 08/923,299 DATE FILED: Sep. abandoned. 4, 1997 49. 5,137,031, Aug. 11, 1992, Urine testing apparatus with SUMMARY: urinarv sediment device; Raouf A. Guirguis, 600/584, 575 [IMAGE BSUM (51) AVAILABLEI

By . . . the separation of the synthon from the L9: polyvalent support it

```
is preferred that the synthon be attached via a chemically the art.
**cleavable**
linker. Upon **cleavage** from the **support**, the
                                                            4. 5,861,532, Jan. 19, 1999, Solid-phase synthesis of N-
**linked** synthons
                                                            alkyl amides;
comprise discrete molecular entities which may be analyzed Edward G. Brown, et al., 564/142; 436/85, 86; 564/133, 134,
for their
                                                            135, 136,
biological activity or physiochemical properties, or which 137, 139 [IMAGE AVAILABLE]
may be. .
                                                                                                                    L10:
    5,876,930, Mar. 2, 1999, Hybridization assay using
                                                            4 of 29
self-quenching
                                                            TITLE:
                                                                            Solid-phase synthesis of N-alkyl amides
fluorescence probe; Kenneth J. Livak, et al., 435/6, 5,
                                                            US PAT NO:
                                                                            5,861,532
                                                                                                     DATE ISSUED:
                                                                                                                    Jan.
91.1. 91.2;
                                                            19, 1999
536/24.3, 24.32, 24.33, 25.3, 25.32, 26.6 [IMAGE AVAILABLE]
                                                                            [IMAGE AVAILABLE]
                                                            APPL-NO:
                                                                            08/813,019
                                                                                                     DATE FILED:
                                                                                                                    Mar.
                                                        L10:4, 1997
2 of 29
TITLE:
               Hybridization assay using self-quenching
                                                            SUMMARY:
fluorescence
                 probe
                                                            BSUM(21)
US PAT NO:
               5,876,930
                                         DATE ISSUED:
                                                        Mar.
2, 1999
                                                             The .
                                                                    . . c) either acylating the N-alkylated solid
               [IMAGE AVAILABLE]
                                                            support-bound
APPL-NO:
               08/558,303
                                         DATE FILED:
                                                        Nov.linker, thereby generating an N-alkylated solid-support
15, 1995
                                                            bound amide, or
REL-US-DATA:
               Continuation of Ser. No. 340,558, Nov. 16,
                                                            sulfonylating the N-alkylated solid **support**-bound
                                                            **linker**, thereby
1994, Pat. No.
                 5,538,848.
                                                            generating an N-alkylated solid-support bound sulfonamide;
SUMMARY:
                                                            **cleaving** the N-alkylated solid support bound amide or
                                                            sulfonamide,
BSUM(28)
                                                            thereby generating the N-substituted carboxamide product or
                                                            sulfonamide
 The linkages between the solid **support**, the **linker**product, respectively.
and the probe
are preferably not **cleaved** during removal of base
                                                            5. 5,859,233, Jan. 12, 1999, Synthons for synthesis of
protecting groups
                                                            oligonucleotide
under basic conditions at high temperature. Examples of
                                                            N3-P5 phosphoramidates; Bernard L. Hirschbein, et al.,
                                                            536/26.1, 26.12,
linkages include carbamate and amide. .
                                                            26.14 [IMAGE AVAILABLE]
DETDESC:
                                                                                                                    L10:
                                                            5 of 29
DETD(15)
                                                            TITLE:
                                                                           Synthons for synthesis of oligonucleotide
                                                            N3-P5
 The linkages between the solid **support**, the **linker**
                                                                             phosphoramidates
and the probe
                                                            US PAT NO:
                                                                           5,859,233
                                                                                                     DATE ISSUED:
                                                                                                                    Jan.
are preferably not **cleaved** during removal of base
                                                            12, 1999
protecting groups
                                                                            [IMAGE AVAILABLE]
under basic conditions at high temperature. Examples of
                                                            APPL-NO:
                                                                           08/771,789
                                                                                                     DATE FILED:
                                                                                                                    Dec.
preferred
                                                            20, 1996
linkages include carbamate and amide. .
                                                            REL-US-DATA:
                                                                           Continuation-in-part of Ser. No. 663,918,
                                                            Jun. 14, 1996,
3. 5,874,532, Feb. 23, 1999, Method for solution phase
                                                                             which is a continuation-in-part of Ser.
synthesis of
                                                            No. 603,566,
oligonucleotides and peptides; Wolfgang Pieken, et al.,
                                                                             Feb. 21, 1996, Pat. No. 5,684,143.
530/338, 322;
536/25.3, 25.34; 562/433 [IMAGE AVAILABLE]
                                                            DETDESC:
                                                        L10: DETD(19)
3 of 29
TITLE:
               Method for solution phase synthesis of
                                                             Even .
                                                                       . phase oligonucleotide synthesis which
oligonucleotides
                                                            involve irreversible
                 and peptides
                                                            coupling steps, considerable guidance in making selections
US PAT NO:
               5,874,532
                                        DATE ISSUED:
                                                        Feb. concerning
23, 1999
                                                            coupling conditions, protecting groups, solid phase
               [IMAGE AVAILABLE]
                                                            **supports**,
                                                        Jan.**linking** groups, deprotection reagents, reagents to
APPL-NO:
               08/780,517
                                        DATE FILED:
8, 1997
                                                            **cleave**
                                                            products from solid phase supports, purification of
DETDESC:
                                                            product, and the
                                                            like, in the context of the present invention can be. .
DETD(176)
                                                            6. 5,846,731, Dec. 8, 1998, Peralkylated oligopeptide
The . . . can contain a cleavable linker between the
                                                            mixtures; Richard
dienophile
                                                            A. Houghten, et al., 435/7.1, 7.2, 7.32; 436/501, 518, 536;
moiety and the resin or membrane, such as an amide bond.
                                                            530/323, 332,
                                                            333, 334, 345 [IMAGE AVAILABLE]
**cleavable** linker allows facile regeneration of the
dienophile
                                                                                                                    L10:
**support**. **Linkers** such as these are well known to
                                                            6 of 29
those skilled in
                                                            TITLE:
                                                                           Peralkylated oligopeptide mixtures
```

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DATE ISSUED:
                                                         Dec. Even . . . phase oligonucleotide synthesis which
8, 1.998
                                                             involve irreversible
                [IMAGE AVAILABLE]
                                                             coupling steps, considerable guidance in making selections
                08/079,144
APPL-NO:
                                         DATE FILED:
                                                         Jun. concerning
17, 1993
                                                             coupling conditions, protecting groups, solid phase
                                                             **supports**,
SUMMARY:
                                                             **linking** groups, deprotection reagents, reagents to
                                                             **cleave**
BSÚM(130)
                                                             products from solid phase supports, purification of
                                                             product, and the
 Once . .
            . dichloromethane, and the support-linked
                                                             like, in the context of the present invention can be. .
peralkylated
peptide set (mixture pool) is then dried. The peralkylated 9. 5,821,130, Oct. 13, 1998, Combinatorial
                                                             dihydrobenżopyran library;
oligopeptide
sets can then be individually **cleaved** from the solid
                                                             John J. Baldwin, et al., 436/518, 523, 524, 525, 526, 527,
supports to
                                                             528, 529, 530,
provide free peralkylated oligopeptide sets, if desired, or 531; 564/183, 184, 186 [IMAGE AVAILABLE]
a solid
**support**-**linked** (-coupled) peralkylated oligopeptide
                                                                                                                     L10:
set can be
                                                             9 of 29
used without **cleavage** from the support.
                                                             TITLE:
                                                                            Combinatorial dihydrobenzopyran library
                                                             US PAT NO:
                                                                            5,821,130
                                                                                                      DATE ISSUED:
                                                                                                                     Oct.
7. 5,840,485, Nov. 24, 1998, Topologically segregated,
                                                             13, 1998
encoded solid
                                                                            [IMAGE AVAILABLE]
phase libraries; Michal Lebl, et al., 435/6, 7.1; 436/518; APPL-NO:
                                                                                                      DATE FILED:
                                                                            08/552,698
                                                                                                                     Nov.
530/300, 323;
                                                             3, 1995
536/23.1 [IMAGE AVAILABLE]
                                                             REL-US-DATA:
                                                                            Continuation-in-part of Ser. No. 436,120,
                                                             May 8, 1995,
                                                        L10:
                                                                              abandoned, which is a continuation-in-part
7 of 29
                                                             of Ser. No.
TITLE:
               Topologically segregated, encoded solid
                                                                              239,302, May 6, 1994, abandoned.
phase libraries
US PAT NO:
               5,840,485
                                         DATE ISSUED:
                                                        Nov. SUMMARY:
24, 1998
                [IMAGE AVAILABLE]
                                                             BSUM(157)
APPL-NO:
               08/249,830
                                         DATE FILED:
                                                        May
26, 1994
                                                              Compounds . . . UV light (.about.360 nm) in polar
REL-US-DATA:
               Continuation-in-part of Ser. No. 68,327, May solvents such as
27, 1993,
                                                             DMSO, H.sub.2 O, or a lower alkanol such as MeOH to
                 abandoned.
                                                             **cleave** the
                                                             compounds of Formula II from the **support**/**linker**
SUMMARY:
                                                             complex.
BSUM(9)
                                                             10. 5,763,193, Jun. 9, 1998, Peralkylated oligopeptide
                                                             mixtures; Richard
 5.3 DEVELOPMENT AND USE OF **SEPARATE** PHASE SYNTHESIS
                                                             A. Houghten, et al., 435/7.1, 7.2, 7.21; 436/501, 518
**SUPPORTS** AND
                                                             [IMAGE AVAILABLE]
**LINKERS** IN ENCODED MOLECULAR LIBRARY SYNTHESES
                                                                                                                     L10:
DETDESC:
                                                             10 of 29
                                                             TITLE:
                                                                            Peralkylated oligopeptide mixtures
DETD(48)
                                                             US PAT NO:
                                                                            5,763,193
                                                                                                      DATE ISSUED:
                                                                                                                     Jun.
                                                             9, 1998
 5.3 Development and Use of **Separate** Phase Synthesis
                                                                            [IMAGE AVAILABLE]
**Supports** and
                                                             APPL-NO:
                                                                            08/577,846
                                                                                                      DATE FILED:
                                                                                                                     Dec.
**Linkers** in Encoded Molecular Library Syntheses
                                                             22, 1995
                                                             REL-US-DATA:
                                                                            Division of Ser. No. 257,782, Jun. 9, 1994,
8. 5,824,793, Oct. 20, 1998, Solid phase synthesis of
                                                             Pat. No.
oligonucleotide
                                                                              5,480,971, which is a continuation-in-part
N3'-P5' phosphoramidates; Bernard L. Hirschbein, et al.,
                                                            of Ser. No.
536/25.34, 25.3,
                                                                              79,144, Jun. 17, 1993.
25.33 [IMAGE AVAILABLE]
                                                            SUMMARY:
                                                        L10:
8 of 29
                                                             BSUM(153)
TITLE:
               Solid phase synthesis of oligonucleotide
N3'-P5'
                                                             Once .
                                                                        . (IPA), three with DCM and one with methanol
                 phosphoramidates
                                                             (MeOH) prior
US PAT NO:
               5,824,793
                                         DATE ISSUED:
                                                        Oct. to drying. The peralkylated oligopeptide sets can then be
20, 1998
                                                             individually
               [IMAGE AVAILABLE]
                                                             **cleaved** from the solid supports to provide free
APPL-NO:
               08/663.918
                                         DATE FILED:
                                                        Jun. peralkylated
14. 1996
                                                            oligopeptide sets, if desired, or a solid **support**-
               Continuation-in-part of Ser. No. 603,566,
REL-US-DATA:
                                                             **linked**
Feb. 21, 1996,
                                                            (-coupled) peralkylated oligopeptide set can be used
                 Pat. No. 5,684,143.
                                                            without **cleavage**
                                                            from the support.
DETDESC:
                                                            11. 5,756,810, May 26, 1998, Process of preparing 3-nitro
DETD(18)
                                                            benzoate
                                                            compounds in lower alkanol; John J. Baldwin, et al.,
```

560/20, 23 [IMAGE

US PAT NO:

5,846,731

AVAILABLE]			1.10	314.7, 361.1,	299, 309, 311, 313, 31		•			
11 of 29 TITLE: compounds in	Process of preparing 3-lower	nitro benzoate	L10: 361.5, 362.1, 362.5, 364.1, 412, 413, 414, 440, 441, 443, 444, 446, 465, 466, 467, 518, 519, 523, 524, 530, 531, 542, 546 [IMAGE AVAILABLE]							
US PAT NO: 26, 1998	alkanol 5,756,810	DATE ISSUED:	May	•			L10:			
APPL-NO:	[IMAGE AVAILABLE] 08/714,065	DATE FILED:	Sep	TITLE:	Pyrrolidine-containing monomers and					
11, 1996 PCT-NO:	PCT/US95/03223	PCT-FILED:		US PAT NO: .3, 1998	5,714,606	DATE ISSUED:	Feb.			
10, 1995	•	371-DATE:		. APPL-NO:	[IMAGE AVAILABLE] 08/669,505	DATE FILED:	7. u.a			
11, 1996		102(E)-DATE:	_	15, 1996 . PCT-NO:	PCT/US95/00356	PCT-FILED:	Aug.			
11, 1996 PCT-PUB-NO:	WO95/24186	PCT-PUB-DATE:	_	11, 1995		371-DATE:	Jan. Aug.			
14, 1995				15, 1996		102(E)-DATE:	Aug.			
SUMMARY:				15, 1996 PCT-PUB-NO:	WO95/18792	PCT-PUB-DATE:	•			
BSUM(137)				13, 1995 REL-US-DATA:	Continuation-in-part o					
light	Y. Compound 7 is then ei		UV	Jan. 11, 1994,	Pat. No. 5,519,134.	1 0011 100,1	J4,			
cleave th				DETDESC:	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,					
protected for **support**/* TFA/thioaniso	<pre>m of the compounds of For *linker** complex or firs le/EDT</pre>	mula II from the t treated with	•	DETD(19)						
to remove the protecting groups on the R.sup.2 sidechai and then exposed to UV				possible because						
_	12. 5,723,591, Mar. 3, 1998, Self-quenching fluorescen				the chemical reaction which defines the nature of the linkage is					
probe; Kenneth				nce **separate** from the attachment of the monomer to the reactive group on the solid **support** (whether **linker** or the previous						
AVAILABLE)		, 23.3, 23.32 (1)	HAGE	monomer).	when a phosphoramidite r	•				
12 of 29		• •	L10:	with tetrazole	he solid support which.		ed			
TITLE: US PAT NO:	Self-quenching fluoresco 5,723,591	ence probe DATE ISSUED:	Mar			•				
3, 1998	[IMAGE AVAILABLE]	J. 11 1000 D.	<pre>Mar.14. 5,714,332, Feb. 3, 1998, Anti .alphagal screening technique; Alexander R. Lussow, et al., 435/7.1, 7.2, 7.21; 436/519 Nov.530/300 [IMAGE AVAILABLE]</pre>							
APPL-NO: 15, 1995	08/559,405	DATE FILED: '								
REL-US-DATA: 1994, Pat. No	Continuation of Ser. No.	340,558, Nov.	16,							
	5,538,848.			14 of 29 TITLE:	Dati alaba asl		L10:			
SUMMARY:				US PAT NO: 3, 1998	Anti .alphagal screer 5,714,332	DATE ISSUED:	Feb.			
BSUM (28)				APPL-NO:	[IMAGE AVAILABLE]					
The linkages and the probe	between the solid **suppo	ort**, the **lin	ker**	22, 1996	08/740,166	DATE FILED:	Oct.			
protecting gro				SUMMARY:						
preferred	onditions at high temperat		f	BSUM(20)						
linkages inclu	linkages include carbamate and amide				<pre>In of the chain while bound to a solid surface, which may be a</pre>					
DETDESC:				particle, silicon chip, or other convenient solid **support**. The						
DETD(15)				**linkage** whi	ch is involved will nor					
The linkages and the probe	between the solid **suppo	rt**, the **link	cer**	photolytically desired compoun		**release** the	!			
protecting gro	/ not **cleaved** during r oups onditions at high temperat			from the suppor developed for	t. A wide variety of te		en			
preferred	de carbamate and amide.									
	5, Feb. 3, 1998, Pyrrolidi			15. 5,702,672, Dec. 30, 1997, Apparatus and method for multiple simultaneous synthesis; Sheila H. H. DeWitt, et al.,						
monomers and	car L. Acevedo, et al., 54	_		422/131, 130, 1	96:					
244, 262,	. ,		,	.,		· · · · · · · · · · · · · · · · · · ·				

L10:

L10: 15 o∉ 29 17 of 29 TITLE: Apparatus and method for multiple TITLE: Synthesis of combinatorial libraries simultaneous synthesis US PAT NO: 5,663,046 DATE ISSUED: Sep. US PAT NO: 5,702,672 DATE ISSUED: Dec. 2, 1997 30, 1997 [IMAGE AVAILABLE] [IMAGE AVAILABLE] APPL-NO: 08/263,804 DATE FILED: Jun. APPL-NO: 08/540,512 DATE FILED: Oct. 22, 1994 10, 1995 REL-US-DATA: Continuation-in-part of Ser. No. 430,696, SUMMARY: Apr. 28, 1995, Pat. No. 5,612,002, which is a division of BSUM(71) Ser. No. 217,347, Mar. 24, 1994, abandoned, which The . . . Y. Compound 7 is then either exposed to UV is a division liaht of Ser. No. 12,557, Feb. 2, 1993, Pat. No. (.about.360 nm) in a lower alkanol such as MeOH to 5,324,483, **cleave** the which is a continuation-in-part of Ser. protected form of the compounds of Formula II from the No. 958,383, **support**/**linker** complex or first treated with Oct. 8, 1992, abandoned. TFA/thioanisole/EDT to remove the protecting groups on the R.sup.2 sidechains DETDESC: and then exposed to UV. . . DETD(252) 18. 5,635,598, Jun. 3, 1997, Selectively cleavabe linners The three possible **cleavage** modes are illustrated. based on **Cleavage** 1 iminodiacetic acid esters for solid phase peptide represents the third building block attacking the solid synthesis; Michal Lebl, et al., 530/334, 343, 345 [IMAGE AVAILABLE] **linkage** to **cleave** the final molecule. This provides structural L10: vaiation at the former site of attachment to the support. 18 of 29 **Cleavage** 2 TITLE: Selectively cleavabe linners based on represents a distal functionality attacking the solid iminodiacetic acid **support** esters for solid phase peptide synthesis **linkage** to **cleave** the final molecule as a cyclized US PAT NO: 5,635,598 DATE ISSUED: Jun. product. 3, 1997 **Cleavage** 3 represents a **cleavage** by an invariant [IMAGE AVAILABLE] agent. This APPL-NO: 08/263,289 DATE FILED: Jun. provides a constant functional group at the former site of 21, 1994 attachment to Continuation-in-part of Ser. No. 81,997, REL-US-DATA: the support. ##STR2## Jun. 23, 1993, abandoned, which is a continuation-in-part 16. 5,688,997, Nov. 18, 1997, Process for preparing of Ser. No. intermediates for a 80,388, Jun. 21, 1993, abandoned. combinatorial dihydrobenzopyran library; John J. Baldwin, et al.. SUMMARY: 562/435; 435/7.1; 560/21 [IMAGE AVAILABLE] BSUM (45) L10: 16 of 29 The . . . directed to solid phase supports comprising TITLE: Process for preparing intermediates for a more than one combinatorial cleavable linker, in which at least one such linker can be dihydrobenzopyran library **cleaved** US PAT NO: 5,688,997 DATE ISSUED: Nov. with formation of a cyclic structure, e.g., a 18, 1997 diketopiperazine, attached [IMAGE AVAILABLE] to the solid phase **support**. The **linkers** can further APPL-NO: 08/482,488 DATE FILED: Jun.comprise a 7, 1995 linker such that upon **cleavage**, the diketopiperazine is REL-US-DATA: Division of Ser. No. 436,120, May 8, 1995, attached to which is a the **released** peptide. In a further embodiment, the continuation-in-part of Ser. No. 239,302, ester bond linkage May 6, 1994, can be to a reactive carboxylic acid, such as abandoned. hydroxymethylbenzoic acid... SUMMARY: DETDESC: BSUM(202) DETD(19) Compounds . . . UV light (.about.360 nm) in polar solvents such as

DMSO, H.sub.2 O, or a lower alkanol such as MeOH to

compounds of Formula II from the **support**/**linker**

17. 5,663,046, Sep. 2, 1997, Synthesis of combinatorial

J. Baldwin, et al., 435/6, 7.1; 436/501, 518, 531, 533;

cleave the

libraries; John

536/18.5, 25.3 [IMAGE AVAILABLE]

530/333, 334;

complex.

alcohol upon formation of a diketopiperazine, which remains on the solid phase **support**. Such **linkers** are termed herein "diketopiperazine (DKP) linkers." The present invention is based in part on the observation that peptide coupled to. . .

In one embodiment, the linkers of the invention

release a peptide

19. 5,618,825, Apr. 8, 1997, Combinatorial sulfonamide library; John J.

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Baldwin, et al., 514/317, 330; 546/227, 229, 232, 233, 234,
                                                                              2, 1993, Pat. No. 5,324,483, Jun. 28,
235; 548/543,
                                                            1994, which is a
556, 569 [IMAGE AVAILABLE]
                                                                              continuation-in-part of Ser. No. 958,383,
                                                            Oct. 8, 1992,
                                                        L10:
                                                                              abandoned.
19 of 29
TITLE:
               Combinatorial sulfonamide library
                                                            DETDESC:
US PAT NO:
               5,618,825
                                        DATE ISSUED:
                                                        Apr.
8, 1997
                                                            DETD(292)
               [IMAGE AVAILABLE]
                                                        Jun. The three possible **cleavage** models are illustrated.
APPL-NO:
               08/482,489
                                         DATE FILED:
7, 1995
                                                            **Cleavage** 1
REL-US-DATA:
               Division of Ser. No. 212,024, Mar. 11, 1994 reprints the third building block attacking the solid
                                                            **support**
SUMMARY:
                                                            **linkage** to **cleave** the final molecule, This provides
                                                            structural
                                                            variation at the former site of attachment to the support.
BSUM(112)
                                                            **Cleavage** 2
 The .
       . . Y. Compound 7 is then either exposed to UV
                                                            represents a distal functionality attacking the solid
light
                                                            **support**
(.about.360 nm) in a lower alkanol such as MeOH to
                                                            **linkage** to **cleave** the final molecule as a cyclized
**cleave** the
                                                            product.
protected form of the compounds of Formula II from the
                                                            **Cleavage** 3 represents a **cleavage** by an invariant
**support**/**linker** complex or first treated with
                                                            agent. This
TFA/thioanisole/EDT
                                                            provides a constant functional group at the former site of
to remove the protecting groups on the R.sup.2 sidechains
                                                            attachment to
and then
                                                            the support. ##STR2##
exposed to UV. . .
                                                            22. 5,565,173, Oct. 15, 1996, Apparatus and method for
20. 5,587,471, Dec. 24, 1996, Method of making
                                                            multiple
oligonucleotide
                                                            simultaneous synthesis; Sheila H. H. DeWitt, et al.,
libraries; Phillip D. Cook, et al., 536/25.3, 25.4, 25.41
                                                            422/131, 130, 196;
[ IMAGE
                                                            435/304.1, 305.2 [IMAGE AVAILABLE]
AVAILABLE 1
                                                                                                                    L10:
                                                        L10:22 of 29
20 of 29
                                                            TITLE:
                                                                           Apparatus and method for multiple
TITLE:
               Method of making oligonucleotide libraries simultaneous synthesis
US PAT NO:
              5,587,471
                                        DATE ISSUED:
                                                       Dec. US PAT NO:
                                                                           5,565,173
                                                                                                     DATE ISSUED:
                                                                                                                    Oct.
24, 1996
                                                            15, 1996
               [IMAGE AVAILABLE]
                                                                           [IMAGE AVAILABLE]
               08/179,972
APPL-NO:
                                        DATE FILED:
                                                        Jan. APPL-NO:
                                                                           08/461,998
                                                                                                     DATE FILED:
                                                                                                                    Jun.
11, 1994
                                                            5, 1995
                                                            REL-US-DATA:
                                                                           Continuation of Ser. No. 430,696, Apr. 28,
SUMMARY:
                                                            1995, which is
                                                                             a continuation of Ser. No. 217,347, Mar.
BSUM(4)
                                                            24, 1994,
                                                                             abandoned, which is a division of Ser. No.
There . . . support-coupled monomeric repeating units, 12,557, Feb.
such as amino
                                                                             2, 1993, Pat. No. 5,324,483, Jun. 28,
acids, by reacting the monomeric units with solid supports 1994, which is a
                                                                             continuation-in-part of Ser. No. 958,383,
solid **supports** **linked** to the monomeric units to
                                                            Oct. 8, 1992.
form a reaction
                                                                             abandoned.
product pool. Thereafter the reaction pool is **separated**
into a number
                                                            DETDESC:
of aliquots of equal weight and the process is repeated to
produce
                                                            DETD(254)
peptides of a desired length.
                                                             The three possible **cleavage** model are illustrated.
21. 5,567,391, Oct. 22, 1996, Apparatus for multiple
                                                            **Cleavage** 1
                                                            represents the third building block attacking the solid
simultaneous
synthesis; Sheila H. H. DeWitt, et al., 422/131, 130, 196; **support**
435/304.1,
                                                            **linkage** to **cleave** the final molecule. This provides
305.2 [IMAGE AVAILABLE]
                                                            structural
                                                            variation at the former site of attachment to the support.
                                                        L10: **Cleavage** 2
21 of 29
                                                            represents a distal functionality attacking the solid
TITLE:
               Apparatus for multiple simultaneous
                                                            **support**
                                                            **linkage** to **cleave** the final molecule as a cyclized
synthesis
US PAT NO:
               5,567,391
                                        DATE ISSUED:
                                                        Oct.product.
22, 1996
                                                            **Cleavage** 3 represents a **cleavage** by an invariant
               [IMAGE AVAILABLE]
                                                            agent. This
APPL-NO:
               08/464,161
                                        DATE FILED:
                                                       Jun. provides a constant functional group at the former site of
5, 1995
                                                            attachment to
REL-US-DATA:
               Continuation of Ser. No. 430,696, Apr. 28, the support. ##STR2##
1995, which is
                 a continuation of Ser. No. 217,347, Mar.
                                                           23. 5,554,501, Sep. 10, 1996, Biopolymer synthesis using
24, 1994,
                                                            surface
                 abandoned, which is a division of Ser. No. activated biaxially oriented polypropylene; Peter J.
12,557, Feb.
                                                            Coassin, et al.,
                                                            435/6; 436/63, 89, 94; 530/334; 536/25.3 [IMAGE AVAILABLE]
```

```
APPL-NO:
                                                                           08/088,622
                                                                                                     DATE FILED:
                                                                                                                    Jul.
                                                       L10:6, 1993
23 of 29
                                                            REL-US-DATA:
                                                                           Continuation of Ser. No. 757,555, Sep. 11,
TITLE:
               Biopolymer synthesis using surface activated 1991,
biaxially
                                                                             abandoned, which is a continuation of Ser.
                 oriented polypropylene
                                                            No. 173,127,
                                        DATE ISSUED:
US PAT NO:
                                                                             Mar. 24, 1988, abandoned, which is a
               5,554,501
                                                       Sep.
10, 1996
                                                                             continuation-in-part of Ser. No. 126,564,
               [IMAGE AVAILABLE]
                                                            Nov. 30, 1987,
APPL-NO:
               08/145,939
                                        DATE FILED:
                                                       Oct.
                                                                             abandoned.
29, 1993
REL-US-DATA:
               Continuation-in-part of Ser. No. 971,100,
                                                            DETDESC:
Oct. 29, 1992,
                 abandoned.
                                                            DETD(34)
DETDESC:
                                                             A . . . to remove protecting groups on the nucleotide
                                                            bases
DETD(64)
                                                            (treatment with concentrated ammonia at 55.degree. C. for 6
                                                            to 10 hours)
Additionally, . . . be utilized in conjunction with
                                                            **cleave** this linkage readily. If the oligonucleotide is
                                                            to remain
spacer arms for the synthesis of biopolymers. These can be bound to the **support** the **linkage** to the 3'-hydroxyl
amenable to
                                                            group must be
either non-**cleavage** or **cleavage** protocols for non- changed to one not **cleaved** under these conditions.
removal or
                                                            Suitable
removal of the synthesized biopolymer from the polymer
                                                            functional groups through which the 3'-OH may be attached
**support*
                                                            include ether
**Linkers** and spacer arms applicable to the synthesis of linkages, phosphate triesters, phosphate diesters. . .
biopolymers,
particularly oligonucleotides and peptides, are well known 26. 5,324,483, Jun. 28, 1994, Apparatus for multiple
                                                            simultaneous
and varied and
will. . .
                                                            synthesis; Donna R. Cody, et al., 422/131, 99, 101, 104
                                                            [IMAGE AVAILABLE]
24. 5,480,971, Jan. 2, 1996, Peralkylated oligopeptide
mixtures: Richard
                                                                                                                    L10:
A. Houghten, et al., 530/328, 329 [IMAGE AVAILABLE]
                                                            26 of 29
                                                            TITLE:
                                                                           Apparatus for multiple simultaneous
                                                       L10: synthesis
24 of 29
                                                            US PAT NO:
                                                                           5,324,483
                                                                                                     DATE ISSUED:
                                                                                                                    Jun.
TITLE:
               Peralkylated oligopeptide mixtures
                                                            28, 1994
US PAT NO:
               5,480,971
                                        DATE ISSUED:
                                                       Jan.
                                                                           [IMAGE AVAILABLE]
2, 1996
                                                            APPL-NO:
                                                                           08/012,557
                                                                                                     DATE FILED: . Feb.
               [IMAGE AVAILABLE]
                                                            2, 1993
APPL-NO:
               08/257,782
                                        DATE FILED:
                                                       Jun. REL-US-DATA:
                                                                           Continuation-in-part of Ser. No. 958,383,
9, 1994
                                                            Oct. 8, 1992,
REL-US-DATA:
               Continuation-in-part of Ser. No. 79,144,
                                                                             abandoned.
Jun. 17, 1993.
                                                            DETDESC:
SUMMARY:
                                                            DETD(254) -
BSUM(150)
                                                             The three possible **cleavage** modes are illustrated.
Once .
           . (IPA), three with DCM and one with methanol
                                                            **Cleavage** 1
(MeOH) prior
                                                            represents the third building block attacking the solid
to drying. The peralkylated oligopeptide sets can then be
                                                            **support**
                                                            **linkage** to **cleave** the final molecule. This provides
individually
**cleaved** from the solid supports to provide free
                                                            structural
peralkylated
                                                            variation at the former site of attachment to the support.
oligopeptide sets, if desired, or a solid **support**-
                                                            **Cleavage** 2
**linked**
                                                            represents a distal functionality attacking the solid
(-coupled) peralkylated oligopeptide set can be used
                                                            **support**
without **cleavage**
                                                            **linkage** to **cleave** the final molecule as a cyclized
from the support.
                                                            product.
                                                            **Cleavage** 3 represents a **cleavage** by an invariant
25. 5,403,711, Apr. 4, 1995, Nucleic acid hybridization
                                                            agent. This
and
                                                            provides a constant functional group at the former site of
amplification method for detection of specific sequences inattachment to
which a
                                                            the support. ##STR2##
complementary labeled nucleic acid probe is cleaved; Joseph
A. Walder, et
                                                            27. 5,286,789, Feb. 15, 1994, Solid phase multiple peptide
al., 435/6, 91.2; 536/24.3 [IMAGE AVAILABLE]
                                                            synthesis;
                                                            David Okrongly, et al., 525/54.11, 54.1, 333.6, 350, 374,
                                                       L10:379; 530/333,
25 of 29
                                                            334, 335, 815, 816 [IMAGE AVAILABLE]
TITLE:
               Nucleic acid hybridization and amplification
method for
                                                                                                                    L10:
                 detection of specific sequences in which a 27 of 29
complementary
                                                            TITLE:
                                                                           Solid phase multiple peptide synthesis
                                                            US PAT NO:
                                                                           5,286,789
                 labeled nucleic acid probe is cleaved
                                                                                                    DATE ISSUED:
                                                                                                                    Feb.
US PAT NO:
               5,403,711
                                        DATE ISSUED:
                                                       Apr. 15, 1994
4, 1995
                                                                           [IMAGE AVAILABLE]
```

[IMAGE AVAILABLE]

```
APPL-NO:
                 08/041,901
                                           DATE FILED:
                                                          Apr. 326, 327, 351, 387.9, 389.2; 930/10, 141, DIG.811 [IMAGE
. -2, 1393
                                                              AVAILABLE]
  REL-US-DATA:
                 Continuation of Ser. No. 671,671, Mar. 19,
  1991,
                                                                                                                       L10:
                   abandoned, which is a continuation of Ser. 29 of 29
 No. 357,987,
                                                              TITLE:
                                                                              Antibodies to human interleukin-2 induced by
                   May 26, 1989, abandoned.
                                                              synthetic
                                                                                polypeptides
 ABSTRACT:
                                                              US PAT NO:
                                                                              4,636,463
                                                                                                        DATE ISSUED:
                                                                                                                       Jan.
 Methods .

    cyclical addition of protected monomers.

                                                              13, 1987
 Reagents are
                                                                              [IMAGE AVAILABLE]
 specifically selected to allow for efficient reproducible
                                                              APPL-NO:
                                                                              06/597,179
                                                                                                       DATE FILED:
                                                                                                                       Apr.
 addition, while
                                                              5, 1984
 maintaining transparency of the **support**. **Linkers**
 are provided
                                                              DETDESC:
 which permit retention of the oligopeptide to the surface
 or **release**
                                                              DETD(108)
 of the oligopeptide at completion of the preparation of the
 oligopeptide.
                                                               When .
                                                                          . a variety of procedures. In any of those
 The oligopeptide bound to the support finds use in. . .
                                                              procedures, the
                                                              reversibly linked complex is dissociated into its component
 28. 5,137,031, Aug. 11, 1992, Urine testing apparatus withparts of
 urinary
                                                               **support**-**linked** antibody and IL-2 followed by
 sediment device; Raouf A. Guirguis, 600/584, 575 [IMAGE
                                                              **separating** the
 AVAILABLE]
                                                              IL-2 from the linked-antibody to provide the purified
                                                              lymphokine free
                                                          L10: from the affinity sorbant.
 28 of 29
 TITLE:
                Urine testing apparatus with urinary
                                                              => log hold
 sediment device
 US PAT NO:
                5,137,031
                                          DATE ISSUED:
                                                         Aug. SESSION WILL BE HELD FOR 30 MINUTES
 11, 1992
                                                              U.S. Patent & Trademark Office SESSION SUSPENDED AT
                [IMAGE AVAILABLE]
                                                              12:00:25 ON 15 MAR 199
 APPL-NO:
                07/567,758
                                          DATE FILED:
                                                         Aug. 9
 15, 1990
                                                              Connection closed by remote host
 REL-US-DATA:
                Continuation-in-part of Ser. No. 408,547,
 Sep. 18, 1989,
                  Pat. No. 5,024,238, and a continuation-in-
 part of Ser.
                  No. 411,041, Sep. 22, 1989, Pat. No.
 4,953,561...
 SUMMARY:
 BSUM (21)
                                   TABLE 6
                        Part-
              용
                        icle
                            Column size
              Cross-
                        size
                            length (cm) .times.
Column **support**
              **linking**
                  Ionic form
                        (.mu.m)
                            i.d. (mm) Examples of
**separations**
Manufacturers
```

Aminex HPX-87N

Sodium

30 .times. 7.8

Raffinose, sucrose,

Bio-

Rade Aminex HPX-87K

29. 4,636,463, Jan. 13, 1987, Antibodies to human interleukin-2 induced by synthetic polypeptides; Amnon Altman, et al., 435/7.92; 210/502.1; 424/85.2; 435/7.93, 7.94, 810, 975; 436/547, 808, 823; 514/14; 530/300,

CLAIMS:

CLMS (10)

- 10. . . . comprising the steps of:
 providing a substrate having a surface with linkers having an active
 site for oligonucleotide synthesis, the linkers being resistant to
 cleavage under cleavage conditions;
 synthesizing an ensemble of sequence-specific oligonucleotides in an
 area of the substrate under a test condition, the oligonucleotides
 having active sites. . .
- 2. 5,679,773, Oct. 21, 1997, Reagants and methods for immobilized polymer synthesis and display; Christopher P. Holmes, 530/334; 430/56; 530/333, 345 [IMAGE AVAILABLE]

US PAT NO:

5,679,773 [IMAGE AVAILABLE]

L12: 2 of 2

SUMMARY:

BSUM(6)

Improved . . . 90/15070) and Fodor et al., PCT Publication No. WO 92/10092, all incorporated herein by reference, disclose methods of forming vast arrays of peptides, oligonucleotides and other polymer sequences using, for example, light-directed synthesis techniques. See also, Fodor et al., Science, 251:767-777 (1991), also incorporated herein by reference for all purposes. These procedures. .

DRAWING DESC:

DRWD(3)

FIGS. . . . linking group. FIGS. 2A and 2B show the reactions which produce the two thiazolidinones. FIGS. 2C and 2D show the HPLC chromatograms of the resulting thiazolidinones and illustrate the purity of each.

DETDESC:

DETD (121)

This method comprises first synthesizing a labeled polymer on a solid support. Subsequent cleavage of the labeled polymer from the support and comparison with known standards provides a confirmation of synthesis fidelity. The precise method of synthesis is not critical and can be carried out by any of the solid phase methods described in the General section. . .

DETDESC:

DETD (123)

The . . . groups, or spacers, L.sup.1 are not critical but are present to permit subsequent synthesis to proceed without interference from the support. However, the bond, spacer or linking group must be cleavable under conditions which do not degrade the synthesized polymer. The linking groups or spacers, when present (i.e., not a bond) are typically 3-50 atoms long and have a. .

DETDESC:

DETD (176)

As . . . both 50% TFA/CH.sub.2 Cl.sub.2 and 95% TFA/H.sub.2 O for one hour. No decomposition of either linking group was observed by HPLC.

DETDESC:

DETD (179)

Commercially . . . with 100 .mu.L of 50% CH.sub.3 CN/H.sub.2 O and again centrifuged. The collected filtrates from each sample were analyzed by HPLC for the presence of thiazolidinone. See FIG. 2. The data indicated that both the thiazolidinones were produced in high purity. .

```
(FILE 'USPAT' ENTERED AT 12:35:49 ON 15 MAR 1999)
                SET HIGH OFF
                ACTIVATE COMLIB/Q
L1
                QUE (LIBRAR#### OR ARRAY# OR MULTIP###### OR COLLECTION#
L2
          14398 S L1
                SET HIGH ON
            144 S L2 AND (CLEAV#### OR RELESE#### OR SEPARAT#####) (15A) (
L3
SUP
             41 S L2 AND (CLEAV#### OR RELESE#### OR SEPARAT#####) (10A) (
L4
SUP
L5
             36 S L4 NOT FD>1995
L6
             19 S L2 AND (CLEAV#### OR RELESE#### OR SEPARAT#####) (10A) (
SUP
             52 S L2 AND (CLEAV#### OR RELESE#### OR SEPARAT#####) (10A) (
L7
SUP
             82 S L2 AND (PHOTOCHEMIC? OR PHOTOLITHOGRAP? OR LIGHT (2W) DI
rs
REC
             25 S L8 AND (CLEAV#### OR RELESE#### OR SEPARAT#####) (10A) (
L9
SUP
              5 S L8 AND (CLEAV#### OR RELESE#### OR SEPARAT#####) (10A) (
L10
SUP
=> S L10 AND gc OR hplc OR MASS SPECTR? OR GEL ELECTROPHORESIS OR PAGE
         14764 GC
         28295 HPLC
        310562 MASS
        225803 SPECTR?
         28300 MASS SPECTR?
                 (MASS (W) SPECTR?)
        165482 GEL
        23180 ELECTROPHORESIS
         14497 GEL ELECTROPHORESIS
                 (GEL (W) ELECTROPHORESIS)
        118035 PAGE
L11
       164529 L10 AND GC OR HPLC OR MASS SPECTR? OR GEL ELECTROPHORESIS O
```

YUNU 489

 5,843,655, Dec. 1, 1998, Methods for testing oligonucleotide arrays; Glenn McGall, 435/6; 436/518, 527, 528 [IMAGE AVAILABLE]

L10: 1 of 5

TITLE: US PAT NO: Methods for testing oligonucleotide arrays

DATE ISSUED: Dec. 1, 1998

[IMAGE AVAILABLE]

APPL-NO:

08/531,155

DATE FILED:

Sep. 18, 1995

SUMMARY:

BSUM (13)

Also provided are methods of determining the extent of depurination of oligonucleotides synthesized on a substrate by spatially directed oligonucleotide synthesis. One method involves providing a substrate having a surface with linkers having an active site for oligonucleotide synthesis, the linkers being resistant to cleavage under cleavage conditions; synthesizing an ensemble of sequence-specific oligonucleotides in an area of the substrate, the oligonucleotides having active sites for attaching a detectable label; attaching a detectable label to the oligonuleotides in the ensemble; exposing the ensemble to a test condition; exposing the ensemble to cleavage conditions that cause cleavage of depurinated oligonucleotides; and determining the amount of detectable label in the area.

SUMMARY:

BSUM (14)

The other method for testing extent of depurination involves providing a substrate having a surface with linkers having an active site for oligonucleotide synthesis, the linkers being resistant to cleavage under cleavage conditions; synthesizing an ensemble of sequence-specific oligonucleotides in an area of the substrate by spatially directed oligonuclectide synthesis under a test condition, the oligonucleotides having active sites for attaching a detectable label; attaching a detectable label to the active sites; exposing the ensemble to cleavage conditions that cause cleavage of depurinated oligonucleotides; and determining the amount of detectable label in the area.

DETDESC:

DETD(3)

This invention provides methods for optimizing the production, storage and use of oligonucleotide arrays produced by spatially directed oligonucleotide synthesis and, in particular, light-directed oligonucleotide synthesis. The methods involve testing arrays produced under a variety of conditions used in the preparation of substrates, the synthesis of nucleic acids on those substrates and the post-production handling, storage, shipment or use of the manufactured biological chips. The invention also provides the ability to test many conditions on a single chip, allowing greater control over the testing process. Also, the ability to test a variety of combinations of conditions on a single chip provides increased flexibility and screening capacity. As used in quality control procedures for manufacturing oligonucleotide arrays, the methods can involve manufacturing the arrays in high volume, and testing selected arrays for various quality parameters such as nucleotide coupling efficiency; amount of deprotection of oligonucleotides; oligonucleotide integrity, e.g., amount of depurination; or amount of double stranded oligonucleotides in the array. Manufacturing arrays in high volume means manufacturing at least 10, 50, 500, 1000, 2000, 5000 or 10,000 oligonucleotide arrays per day from a single fabricating machine or in a single fabrication facility.

DETDESC:

DETD(5)

In one embodiment oligonucleotide arrays are synthesized at specific locations by light-directed oligonucleotide synthesis. The pioneering techniques of this method are disclosed in U.S. Pat. No. 5,143,854; PCT WO 92/10092; PCT WO 90/15070; and U.S. application Ser. Nos. 08/249,188, 07/624,120, and 08/082,937, incorporated herein by reference for all purposes. The basic strategy of this process is outlined in FIG. 1. The surface of a solid support modified with linkers and photolabile protecting groups (.sup..about. O--X) is illuminated (hv) groups (HO) in the illuminated regions. A 3'-O-phosphoramidite-activated deoxynucleoside (protected at the 5'-hydroxyl with a photolabile group, T--X) is then presented to the surface and coupling occurs at sites that were exposed to light. Following the optional capping of unreacted active sites and oxidation, the substrate is rinsed and the surface is illuminated (hv) through a second mask (M.sub.2), to expose additional hydroxyl groups for coupling to the linker. A second 5'-protected, 3'-O-phosphoramidite-activated deoxynucleoside (C--X) is presented to the surface. The selective photodeprotection and coupling cycles are repeated until the desired set of products is obtained. Photolabile groups are then optionally removed and the sequence is, thereafter, optionally capped. Side chain protective groups, if present, are also removed. Since photolithography is used, the process can be miniaturized to generate high-density arrays of oligonucleotide probes. Furthermore, the sequence of the oligonucleotides at each site is known.

DETDESC:

DETD (59)

In another embodiment, fluorescent probes are employed in combination with CCD imaging systems. Details of this method are described in U.S. application Ser. No. 08/301,051, incorporated herein by reference in its entirely. In many commercially available microplate readers, typically the light source is placed above an array, and a photodiode detector is below the array. For the present methods, the light source can be replaced with a higher power lamp or laser. In one embodiment, the standard absorption geometry is used, but the photodiode detector is replaced with a CCD camera and imaging optics to allow rapid imaging of the array. A series of Raman holographic or notch filters can be used in the optical path to eliminate the excitation light while allowing the emission to pass to the detector. In a variation of this method, a fiber optic imaging bundle is utilized to bring the light to the CCD detector. In another embodiment, the laser is placed below the oligonucleotide array and light directed through the transparent wafer or base that forms the bottom of the oligonucleotide array. In another embodiment, the CCD array is built into the wafer of the oligonucleotide array.

CLAIMS:

CLMS(2)

- 2. A method for determining the amount of depurination of oligonucleotides synthesized on a substrate by spatially directed oligonucleotide synthesis comprising the steps of:
- providing a substrate having a surface with linkers having an active site for oligonucleotide synthesis, the linkers being resistant to cleavage under cleavage conditions;
- synthesizing an ensemble of sequence-specific oligonucleotides in an area of the substrate, the oligonucteotides having active sites for attaching a detectable label;
- attaching a detectable label to the oligonucleotides in the ensemble; exposing the ensemble to a test condition;
- exposing the ensemble to cleavage conditions that cause cleavage of depurinated oligonucleotides; and
- determining the amount of detectable label in the area, said amount of detectable label being a determination of said amount of depurination.

CLAIMS:

CLMS (10)

- 10. A method for determining the amount of depurination of oligonucleotides synthesized on a substrate by spatially directed oligonucleotide synthesis comprising the steps of:
- providing a substrate having a surface with linkers having an active site for oligonucleotide synthesis, the linkers being resistant to cleavage under cleavage conditions;
- synthesizing an ensemble of sequence-specific oligonucleotides in an area of the substrate under a test condition, the oligonucleotides having active sites for attaching a detectable label;
- attaching a detectable label to the active sites;
- exposing the ensemble to cleavage conditions that cause cleavage of depurinated oligonucleotides; and
- determining the amount of detectable label in the area, said amount of detectable label being a determination of said amount of depurination.
- 2. 5,770,455, Jun. 23, 1998, Methods and apparatus for synthesizing labeled combinatorial chemistrylibraries; John Cargill, et al., 436/518; 435/4; 436/524, 525, 526, 527, 528; 530/334 [IMAGE AVAILABLE]

TITLE:

Methods and apparatus for synthesizing labeled

combinatorial chemistrylibraries

5,770,455 US PAT NO:

DATE ISSUED: Jun. 23, 1998

APPL-NO:

[IMAGE AVAILABLE]

REL-US-DATA:

08/480,438 DATE FILED: Jun. 7, 1995 Division of Ser. No. 383,766, Feb. 2, 1995, which is a continuation-in-part of Ser. No. 180,863, Jan. 13, 1994, abandoned, which is a continuation-in-part of Ser. No.

92,863, Jul. 19, 1993, abandoned.

SUMMARY:

BSUM (53)

In another recent development, scientists combined the techniques of photolithography, chemistry and biology to create large collections of oligomers and other compounds on the surface of a substrate (this method is called "VLSIPS.TM."). See, for example, U.S. Pat. No. 5,143,854; PCT Publication No. 90/15070; PCT Publication No. 92/10092 entitled "Very Large Scale Immobilized Polymer Synthesis," Jun. 25, 1992; Fodor et al., "Light-Directed Spatially Addressable Parallel Chemical Synthesis," Science 251: 767-773 (1991); Pease et al., "Light-Directed Oligonucleotide Arrays for Rapid DNA Sequence Analysis, " Proc. Natl. Acad. Sci. 91: 5022-5026 (1994); and Jacobs & Fodor, "Combinatorial Chemistry: Applications of Light-Directed Chemical Synthesis," Trends. Biotechnology 12(1): 19-26 (1994), each of which is incorporated herein by reference.

SUMMARY:

BSUM (98)

The present invention also relates to methods and apparatus for synthesizing labeled libraries of random oligomers. The random oligomers are generally synthesized on synthesis supports, but may be cleaved from these supports or synthesized in solution phase to provide a soluble library. In a preferred embodiment the oligomers are composed of a set of monomers, the monomers being any member of the set of atoms or molecules that can be joined together to form an oligomer or polymer. The library is then screened to isolate individual oligomers that bind to a receptor or possess some desired property. In a preferred embodiment, each oligomer structure in the library is unique.

3. 5,679,773, Oct. 21, 1997, Reagants and methods for immobilized polymer synthesis and display; Christopher P. Holmes, 530/334; 430/56; 2 530/333, 345 [IMAGE AVAILABLE]

L10: 3 of 5

TITLE: Reagants and methods for immobilized polymer synthesis and

display US PAT NO:

5,679,773

DATE ISSUED:

Oct. 21, 1997

APPL-NO:

[IMAGE AVAILABLE] 08/374,492

DATE FILED:

Jan. 17, 1995

SUMMARY:

BSUM (6)

Improved methods of forming large arrays of oligonucleotides, peptides and other polymer sequences in a short period of time have been devised. Of particular note, Pirrung et al., U.S. Pat. No. 5,143,854 (see also PCT Application No. WO 90/15070) and Fodor et al., PCT Publication No. WO 92/10092, all incorporated herein by reference, disclose methods of forming vast arrays of peptides, oligonucleotides and other polymer sequences using, for example, light-directed synthesis techniques. See also, Fodor et al., Science, 251:767-777 (1991), also incorporated herein by reference for all purposes. These procedures are now referred to as VLSIPS.TM. procedures.

DETDESC:

DETD (121)

This method comprises first synthesizing a labeled polymer on a solid support. Subsequent cleavage of the labeled polymer from the support and comparison with known-standards provides a confirmation of synthesis fidelity. The precise method of synthesis is not critical and can be carried out by any of the solid phase methods described in the General section above. In order to obtain a solid substrate-bound polymer having the formula above, the synthesis will typically proceed by first attaching a linking group or spacer, L.sup.1, to the solid support.

DETDESC:

DETD (123)

The linking groups, or spacers, L.sup.1 are not critical but are present to permit subsequent synthesis to proceed without interference from the support. However, the bond, spacer or linking group must be cleavable under conditions which do not degrade the synthesized polymer. The linking groups or spacers, when present (i.e., not a bond) are typically 3-50 atoms long and have a surface attaching portion and a functional group for covalent attachment to the label attaching group. The surface attaching portion is that part of L.sup.1 which is directly attached to the solid support. This portion can be attached to the solid support via carbon-carbon bonds using, for example, supports having (poly) trifluorochloroethylene surfaces, or preferably, by siloxane bonds (using, for example, glass or silicon oxide as the solid support). Siloxane bonds with the surface of the support are formed in one embodiment via reactions of surface attaching portions bearing trichlorosilyl or trialkoxysilyl groups. The spacer will also have a site for attachment of the label attaching group. For example, groups which are suitable for attachment to such a group would include amines, hydroxyl, thiol, and carboxyl. Thus, preferred linking groups or spacers, are those molecules derived from aminoalkylsilanes and hydroxyalkylsilanes. In particularly preferred embodiments, the spacer L.sup.1 is derived from bis(2-hydroxyethyl)aminopropyl-triethoxysilane, 2-hydroxyethylaminopropyltriethoxysilane, aminopropyltriethoxysilane or hydroxypropyltriethoxysilane.

4. 5,677,195, Oct. 14, 1997, Combinatorial strategies for polymer synthesis; James L. Winkler, et al., 436/518; 422/134, 149; 435/6, 7.92, 970, 973; 436/89, 527, 528; 530/333, 334, 335; 536/25.3, 25.31, 25.32 [IMAGE AVAILABLE]

L10: 4 of 5

TITLE: Combinatorial strategies for polymer synthesis

US PAT NO: 5,677,195 DATE ISSUED: Oct. 14, 1997

[IMAGE AVAILABLE] DISCL-DATE: Jan. 24, 2012 APPL-NO: 07/980,523 DATE FILED: Nov. 20, 1992

REL-US-DATA: Continuation-in-part of Ser. No. 796,243, Nov. 22, 1991,

Pat. No. 5,384,261, and Ser. No. 874,849, Apr. 24, 1992,

Pat. No. 5,412,087.

SUMMARY:

BSUM (4)

Improved methods of forming large arrays of peptides, oligonucleotides, and other polymer sequences in a short period of time have been devised. Of particular note, Pirrung et al., U.S. Pat. No. 5,143,854 (see also PCT Application No. WO 90/15070) and Fodor et al., PCT Publication No. WO 92/10092, all incorporated herein by reference, disclose methods of forming vast arrays of peptides and other polymer sequences using, for example, light-directed synthesis techniques. See also, Fodor et al., Science (1991) 251:767-777, also incorporated herein by reference for all purposes.

DETDESC:

DETD (86)

By adjusting the thickness of the synthesis support matrix, the quantity of immobilized material in the reaction regions can be controlled. For example, relatively thin support synthesis matrices can be used to produce small amounts of surface bound oligomers for analysis, while thicker support matrices can be used to synthesize relatively large quantities of oligomers which can be cleaved from the support for further use. In the latter embodiment, a collector having dimensions matching the individual synthesis supports can be employed to collect oligomers that are ultimately freed from the reaction matrix.

5. 5,585,275, Dec. 17, 1996, Pilot apparatus for peptide synthesis and screening; Derek Hudson, et al., 436/518; 422/68.1, 99, 129; 436/523, 524, 527, 528, 529, 531; 530/333, 334 [IMAGE AVAILABLE]

TITLE: Pilot apparatus for peptide synthesis and screening US PAT NO: 5,585,275 DATE ISSUED: Dec. 17, 1996

[IMAGE AVAILABLE]

APPL-NO: 08/079,741 DATE FILED: Jun. 18, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 939,065, Sep. 2, 1992.

SUMMARY:

The Affymax "chip" approach described in PCT publication WO90/10570, and in Fodor, P. A. et al, Science, 251 (1991) 767, is a method for multiple peptide synthesis on a solid support which uses synthesis and flourescent detection on the silica surfaces of flow through cells, photolabile protecting groups and photolithographic masking strategies to make arrays. Photolabilely-blocked amino groups are chemically attached (bonded) to a silicon chip, then irradiated through a patterned mask to selectively remove the blocking groups in a pre-arranged pattern. An amino acid will bond by addition only to the irradiation exposed areas. Additional masks are imposed and radiation applied as a prelude to adding second amino acids. Each amino acid added can include a blocking group so that further addition to that site occurs only after irradiation unblocking. Repeating the process with plural masks builds location specific polypeptides. When the chip is exposed to the target molecule, it may stick to one or more locations. By checking coordinates on a map of the chip, the peptide is identified. However, this process does not work with target molecules stuck to, or part of, cells, and there are exposure problems during processing, i.e., some AA's are light sensitive and cannot be used. Further, the reactions at the surface are not complete; for example, where reaction completion is only 90%, by the 6th iteration to obtain a hexapeptide, only half of them will be made properly.

DETDESC:

DETD (21)

Because of the effectiveness of the support system of this invention, the separate zones (one or more support address area(s)) can be functionalized for synthesis of peptides at loadings as low as about 0.001 micromoles per cm.sup.2 usually in the range of from about 0.05 to about 50.mu. mole/area, and 50-100 nmole loading for HPMP winks.